2018-05

Mental Health in UK Biobank - development, implementation and results from an online questionnaire completed by 157,366 participants

Lee, WE

Bjpsych Open
The Royal College of Psychiatrists

Title: Mental Health in UK Biobank – development, implementation and results from an online questionnaire completed by 157,366 participants

Article and Supplementary Material

Katrina A. S. Davis MRCPsych (i) King's College London, Institute of Psychiatry Psychology and Neuroscience, London, United Kingdom (ii) South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, PO Box 005, De Crespigny Park, Denmark Hill, London, UK

Jonathan R. I. Coleman PhD, (i) King's College London, Institute of Psychiatry Psychology and Neuroscience, London, United Kingdom (ii) South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, PO Box 005, De Crespigny Park, Denmark Hill, London, UK

Mark Adams PhD, University of Edinburgh: Division of Psychiatry, University of Edinburgh, Edinburgh, UK

Naomi Allen DPhil, (i) University of Oxford (ii) UK Biobank: UK Biobank, Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery Old Road Campus, Roosevelt Drive, Oxford, UK

Breen, Gerome PhD, (i) King's College London, Institute of Psychiatry Psychology and Neuroscience, London, United Kingdom (ii) South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, PO Box 005, De Crespigny Park, Denmark Hill, London, UK

Breda Cullen DClinPsy, University of Glasgow: Mental Health and Wellbeing , University of Glasgow, The Academic Centre, Gartnavel Royal Hospital , Great Western Road, Glasgow , Scotland, UK

Breda Cullen DClinPsy, University of Glasgow: Mental Health and Wellbeing , University of Glasgow, The Academic Centre, Gartnavel Royal Hospital , Great Western Road, Glasgow , Scotland, UK

Chris Dickens PhD, University of Exeter: Institute of Health Research, University of Exeter Medical School, Exeter, UK

Elaine Fox FBPS, University of Oxford: Department of Experimental Psychology, University of Oxford, Oxford, UK

Nick Graham MRCPsych, University of Glasgow: Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Jo Holliday PhD, (i) University of Oxford (ii) UK Biobank: UK Biobank, Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery Old Road Campus, Roosevelt Drive, Oxford, UK

Louise M Howard PhD, King's College London, Institute of Psychiatry Psychology and Neuroscience: Section of Women's Mental Health, IOPPN, King's College London, David Goldberg Centre, 16 De Crespigny Park, London, UK

Ann John MD, Swansea University: Farr Institute of Health Informatics Research, Swansea University Medical School, Swansea, Wales, UK

William Lee PhD, (i)Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK (ii) Devon Partnership NHS Trust , Exeter, UK.

Rose McCabe PhD, University of Exeter: College House, University of Exeter Medical School, St. Luke's Campus, Exeter, UK

Andrew McIntosh FRCPsych, University of Edinburgh: Division of Psychiatry, University of Edinburgh, Edinburgh, UK

Robert Pearsall DPhil, University of Glasgow: Institute of Health and Wellbeing, University of Glasgow, Glasgow, UKDaniel J. Smith FRCPsych, University of Glasgow: Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Cathie Sudlow FRCPE, (i) University of Edinburgh (ii) UK Biobank: UK Biobank, Centre for Medical informatics, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK

Joey Ward MSc, University of Glasgow: MSc. Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Stan Zammit PhD, (i) University of Bristol (ii) University of Cardiff: Centre for Academic Mental Health, University of Bristol, Oakfield House, Oakfield Grove, Clifton, Bristol, UK & Institute of Psychological Medicine and Clinical Neurosciences, University of Cardiff, Cardiff University School of Medicine, Haydn Ellis Building, Maindy Road, Cardiff, UK

Matthew Hotopf FMedSci, (i) King's College London, Institute of Psychiatry Psychology and Neuroscience, London, United Kingdom (ii) South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, PO Box 005, De Crespigny Park, Denmark Hill, London, UK

Corresponding Author: Matthew Hotopf, (i) King's College London, Institute of Psychiatry Psychology and Neuroscience, London, United Kingdom (ii) South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, PO Box 005, De Crespigny Park, Denmark Hill, London, UK. (Email: matthew.hotopf@kcl.ac.uk) Tel: 020 7848 0120, Fax: 020 7848 5408

Abstract:
Background: UK Biobank is a well-characterised cohort of over 500,000 participants that offers unique opportunities to investigate multiple diseases and risk factors. An online mental health questionnaire completed by UK Biobank participants expands the potential for research into mental disorders.

Methods: An expert working group designed the questionnaire, using established measures where possible, and consulting with a service user group regarding acceptability. Case definitions were defined using operational criteria for lifetime depression, mania, anxiety disorder, psychotic-like experiences and self-harm, and current post-traumatic stress and alcohol use disorders.

Results: 157,366 completed online questionnaires were available by August 2017. Comparison of self-reported diagnosed mental disorder with a contemporary study shows a similar prevalence, despite respondents being of higher average socioeconomic status than the general population across a range of indicators. Thirty-five percent (55,750) of participants had at least one defined syndrome, of which lifetime depression was the most common at 24% (37,434). There was extensive comorbidity among the syndromes. Mental disorders were associated with high neuroticism score, adverse life events and long-term illness; addiction and bipolar affective disorder in particular were associated measures of deprivation.

Conclusions: The questionnaire represents a very large mental health survey in itself, and the results presented here show high face validity, although caution is needed due to selection bias. Built into UK Biobank, these data intersect with other health data to offer unparalleled potential for crosscutting biomedical research involving mental health.

Introduction

UK (United Kingdom) Biobank is a very large, population-based cohort study established to identify the determinants of common life-threatening and disabling conditions.[1] Most of these conditions, like heart disease, stroke and mental disorders, are multifactorial, involving multiple genes of small effect, and complex relationships with environmental exposures. This means large samples are required to study associations between these exposures and disease, and identify targets for treatment and prevention.[2] The utility of traditional epidemiological study designs is often limited by their focus on single disorders or exposures and relatively modest sample sizes.[3] UK Biobank is an open-access resource providing detailed characterisation of over half a million people aged 40-69 years at recruitment, with proposed long term follow-up. Recruitment completed in 2010, along with consent for future contact and linkage to routinely collected health-related data, such as those produced by the NHS. Baseline measures were extensive, from family history to sensory acuity (a searchable breakdown www.ukbiobank.ac.uk), and the resource continues to grow. Earlier this year, genotyping of the whole cohort was complete, blood biomarkers are due next year, and multimodal imaging is underway for 100,000 participants. Locality environmental factors, such as air pollution, are also available. The design of UK Biobank offers the opportunity to examine a wide range of risk factors and outcomes in a sample that has the size to provide the power to detect small effects, making UK Biobank a highly efficient resource for observational epidemiology.

The impact of mental disorders on disability and quality of life is considerable,[4] accounting for the equivalent of over 1.2 million person years lost to disability from mental and substance use disorders in England alone in 2013[5]. Recent work has also highlighted the potential detrimental impact of mental disorders both on physical disease onset and outcomes.[6-8] Having mental health phenotypes available in conjunction with the wealth of other data in the UK Biobank would offer considerable opportunities to study aetiological and prognostic factors. The UK Biobank baseline data collection had limited assessment of mental health, consisting of several questions about mood and a neuroticism scale, expanded for the last 172,729 recruited participants with questions to allow provisional categorisation of mood disorder;[9] however, there was considerable scope for further characterisation of mental disorders among participants.

Characterising mental disorders in a cohort such as UK Biobank poses challenges. Firstly, most mental disorders manifest before age 30 years and have fluctuating courses,[10] so a "snapshot" of disorder status at one point in time, as identified by most screening tools, is likely to be less useful than a "lifetime" history. Secondly, traditional diagnostic approaches to mental disorders, relying upon clinician assessment at interview, would be prohibitively expensive in a cohort of this size. Thirdly, using self-report of diagnosis or data from record linkages relies upon recognition of illness and reflects healthcare usage patterns, whereas many people with mental disorders never seek or receive treatment.[10, 11] In response to these challenges, we developed a dual approach: secondary care record linkage for identification of more severe illnesses such as schizophrenia[12] and self-report of symptoms of common mental disorder, which might not have come to clinical attention. As part of our mental health phenotyping programme we therefore developed an online mental health questionnaire (MHQ) for participants to complete regarding lifetime symptoms of mental disorders. The MHQ aimed to exploit the efficiency of "e-surveys"[13] and provide the detail needed to identify mental health disorders without the need for a clinical assessment.

The present paper aims to describe the development, implementation and results of this questionnaire. We provide descriptive data on the numbers of UK Biobank participants meeting diagnostic criteria for specific disorders, and on the frequency of exposure to risk factors. We also evaluate the likely representativeness of respondents by comparing respondent socio-demographic characteristics to that of the UK population using census data, and comparing self-reported mental disorder diagnosis with the Health Survey for England (HSE) data.[14] This will assist researchers

considering or undertaking epidemiological research evaluate the potential and power of using UK Biobank to look at mental health.

Methods

Questionnaire development

A mental health research reference group formed of approximately 50 individuals (see supplementary material Appendix 1) participated in discussions about a strategy for mental health phenotyping in UK Biobank, including a workshop in January 2015. From this, a smaller steering group was established and led the development of the mental health questionnaire (MHQ). The group recommended that the MHQ should concentrate on depression, as it was likely to represent the greatest burden in the cohort, with some questions about other common disorders, including anxiety, alcohol misuse and addiction, plus risk factors for mental disorder not captured at participants' baseline assessment.

The intention was to create a composite questionnaire out of previously existing and validated measures, taking into account participant acceptability (time, ease of use, and ensuring questions were unlikely to offend), scope for collaborations with international studies (e.g. the Psychiatric Genomics Consortium) through making results comparable, and the need to balance depth and breadth of phenotyping. The base of the questionnaire was the measurement of lifetime depressive disorder using the Composite International Diagnostic Interview Short Form (CIDI-SF),[15] modified to provide lifetime history, as used to identify cases and controls for some existing studies in the Psychiatric Genomics Consortium. The CIDI-SF uses a branching structure with screening questions and skip rules to limit detailed questions to the relevant areas for each participant. Other measures were then added to this, as summarised in supplementary material Table SM1. Where the group were unable to find existing measures that fulfilled these criteria, questions were written or adapted, as indicated in SM1. These sections have not been externally validated, but the questions can be seen, along with the full questionnaire on the UK Biobank website (http://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=22), for researchers to evaluate how they wish to use them.

Testing and ethical approval

The use of branching questions in the MHQ means that those with established and multiple mental disorders have a longer, more detailed, questionnaire. To improve acceptability in this group, we worked with a service user advisory group at the National Institute of Health Research (NIHR) Biomedical Research Centre at the South London and Maudsley (SLaM) NHS Foundation Trust in designing the questionnaire and invitation.[16] We then piloted the questionnaire amongst an online cohort of 14,836 volunteers aged over 50 and living in the UK, who completed the questionnaire as part of signing up to take part in the Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT).[17] Of those who started the questionnaire 98.8% completed it, taking a median time of 15 minutes. Some PROTECT participants commented that they wanted the opportunity to explain why they felt they had experienced symptoms of depression. In response to this, we added a question to the depression section on loss or bereavement, and a free-text box – neither were designed to change diagnostic algorithms, but may add to future analyses.

The questionnaire was approved as a substantial amendment to UK Biobank approval from the North West - Haydock Research Ethics Committee , 11/NW/0382.

Administration to UK Biobank Participants

We incorporated the final MHQ into the UK Biobank web questionnaire platform and presented it to participants as an online questionnaire entitled "thoughts and feelings". We sent participants who

had agreed to email contact a hyperlink to their personalised questionnaire. The invitation explained the importance of collecting further information about mental health and emphasised that UK Biobank was unable to respond to concerns raised by the participant in the questionnaire, instead directing them to several sources of potential support. Participants could skip questions they preferred not to answer, and they could save answers to return to the questionnaire later. We sent reminder emails at two weeks and four months to those who had not started or had partially completed the questionnaire. The MHQ will continue to be available on the participant area of the UK Biobank website, and the annual postal newsletter contains an invitation to log on to the participant area and complete the MHQ that will reach those for whom no email contact was possible. Data from this questionnaire will therefore continue to accrue. The current numbers and aggregate data can be accessed from the public data showcase (http://biobank.ctsu.ox.ac.uk/crystal/label.cgi?id=136). More detail on the roll out and associated communications can be found on the UK Biobank website (http://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=22).

Defining Cases from the MHQ

Case definitions for the evaluation of the responses on the MHQ are detailed in Appendix 2 in supplementary materials. They arose either from the instruments used in the MHQ or by consensus criteria agreed by the working committee who wrote the MHQ. Diagnostic criteria were evaluated for depression (major depressive disorder), hypomania or mania, generalised anxiety disorder (GAD), alcohol use disorder, and post-traumatic stress disorder (PTSD). Addiction to substances and/or behaviour was defined based on self-report alone. Unusual experiences (describing potential symptoms of psychosis) and self-harm were also defined as phenomena that are important for phenotyping, but not disorder-specific. We combined outcomes to divide the cohort into five mood disorder groups, as shown in supplementary material Figure s1

Fulfilling the diagnostic criteria based on a self-report questionnaire does not allow us to rule out other psychiatric disorders, psychological or situational factors that might better explain the symptoms, and may have been elicited in a clinical evaluation. Therefore, we would regard any case classification arising from the MHQ as "likely", rather than confirmed psychiatric disorder. The issue becomes particularly problematic for disorders that are less common in the population, such as bipolar affective disorder, where literature shows that using questionnaires to screen the population may over-estimate prevalence.[18] Therefore, although we report the presence of hypomania/mania symptoms for the whole population, we only make the likely diagnosis of bipolar affective disorder in people with a history of depression, a sub-population where the prevalence of bipolar affective disorder is higher, and therefore screening questionnaires have better positive predictive values.[19]

Analysis and Data Sharing

Data were supplied by UK Biobank on 8th August 2017 under application number 16577. We used R version 3.4.0 and MS Excel for analyses. We report numbers and proportions within the sample, and do not attempt to give population prevalence estimates. The large sample size meant that all 95% confidence intervals were less than 0.3 away from percentage proportions, and are therefore not shown.

The data for tables can be found in online supplementary materials. The code is available from Mendeley Data (Reserved DOI**:** doi:10.17632/kv677c2th4.2). Raw data are available from UK Biobank subject to the usual access procedures (www.ukbiobank.ac.uk).

Role of the funding source

The questionnaire was developed and administered with UK Biobank funding. Individual authors were funded by their institutions and research grants as detailed below. No funding body influenced

the study design or the writing of this article. MH had access to all data through a standard data sharing agreement (Material Transfer Agreement) with UK Biobank and retains final responsibility for the decision to submit the article for publication.

Results

The setting, recruitment and methods of selection of participants in UK Biobank have been published elsewhere.[1, 9] For the mental health questionnaire study, 339,092 participants were sent an email invitation, and 157,366 (46% of those emailed) fully completed the questionnaire by August 2017 – which means that the MHQ currently has 31% coverage of the UK Biobank cohort. Figure 1 shows the flow chart of UK Biobank participants who completed the mental health questionnaire (MHQ). The median time for completion was 14 minutes, and 82% of respondents completed the questionnaire in under 25 minutes.

Insert Figure 1 around here Flowchart of UK Biobank (UKB) participants from invitation to completion of mental health questionnaire (MHQ). Invitations were based on NHS registration, age and location.

Table SM2 in supplementary material shows participant characteristics for all UK Biobank participants and those who completed the MHQ compared to population-level data for UK residents in the same age range. They were different from the whole UK Biobank cohort and the general population by being better educated (e.g. 45% hold a degree vs 32% of UK Biobank participants vs 23% in the census), of higher socio-economic status according to job type, and healthier (longstanding illness or disability 28% vs 32% vs 37%), with lower rates of current smoking.

Insert Table 1 around here Respondent reports of mental health diagnoses by a professional compared to diagnoses reported in the Health Survey for England (HSE) 2014

Table 1 shows that 34% of respondents reported they had received at least one psychiatric diagnosis from a professional at some time, and 12% had received two or more. The most commonly reported diagnosis was depression, followed by “anxiety or nerves”. Data are compared to the Health Survey for England (HSE) because this annual survey aims to report data that is a representative estimate for the population in England through its sample and weighting.[20] The comparison shows that the pattern and prevalence of diagnosis is similar; for example, a depression diagnosis was self-reported by 21% of individuals in both samples, eating disorder by around 1%, and bipolar-related disorders by around 0.5%. The definition in the MHQ differed from that in the HSE for anxiety (MHQ definition was broader) and addiction (MHQ did not require professional diagnosis), and the higher overall prevalence in the UK Biobank MHQ compared to the HSE (35% vs 28%) may be due to those wider definitions.

Insert Table 2 around here Comorbidity between operationally defined syndromes

Table 2 shows that 35% of participants met criteria for one or more operationally defined syndromes. The most common was lifetime depression at 24%, followed by anxiety disorder and alcohol use disorder (both 7%), PTSD (6%), unusual experiences (5%), and self-harm (4%). Hypomania / mania was the least common, at 2% of respondents. Table SM3 in supplementary material shows that women were more likely than men to have a history of one or more of the defined syndromes (39% vs 30%), particularly depression, anxiety and PTSD. Men were more likely than women to have an alcohol use disorder (10% vs 5%) and there was little difference in the rate of report of unusual experiences (both 5%). Table 2 also shows the substantial comorbidity of defined syndromes. Notably, around three-quarters of participants who met criteria for lifetime

anxiety disorder also met criteria for lifetime depression, whilst individuals with PTSD had at least a two-fold increase in lifetime prevalence of all other syndromes. Alcohol use disorder appeared less related to the others.

Insert Table 3 around here Selected personal characteristics, socio-economic factors, risk factors and health behaviours by status for likely lifetime occurrence of operationally defined syndromes (people may be included in more than one category)

The proportion of respondents meeting criteria for the lifetime occurrence of at least one of depression, anxiety, unusual experience and addiction is shown in figure SM1 to vary according to age and gender, from 16% in men over 75 years to 42% in women aged 45-54 years. Table 3 shows that respondents with any of these lifetime syndromes were more likely than those without to live in areas of higher deprivation, especially if they had bipolar disorder or reported addiction. They were also more likely to have had adverse life events and have met criteria for loneliness, and to a lesser extent social isolation. They were more likely to have smoked cigarettes and/or used cannabis, and to have had a "longstanding illness" at baseline (although the presence of a mental disorder may have been the illness to which the participants refer in some cases). Achieving recommended levels of physical activity did not appear to be associated with any of the syndromes.

The supplementary materials have a section on mood disorder, showing the results of analyses of MHQ participants by likely disorder categories (figure MD1). Table MD1 shows the features of these groups. The characteristics of people who meet diagnostic criteria for depression appear to be shared by those with subthreshold depressive symptoms. Table MD2 shows comorbidity, and demonstrates a gradient effect in the presence of a non-depression syndrome rising from 7% in no depression to 43% in recurrent depression. Table MD3 shows an association between the presence of lifetime unipolar depression or bipolar affective disorder and worse scores for current mental health.

Discussion

This paper has described the development, implementation and principal descriptive findings from the UK Biobank Mental Health Questionnaire (MHQ). The implementation of this questionnaire demonstrates that a web-based questionnaire is an acceptable means of collecting mental health information at low cost and large scale. Whilst the data collection methods might force more limited data acquisition than conventional interview methods, with associated uncertainties in true diagnostic categorisation, we suggest that the survey achieved an acceptable trade-off between depth of phenotypic information and scale of sample size.

The MHQ achieved a participation rate of 31% of the original UK Biobank participants and 46% of those emailed. This response rate is substantially higher than previous UK Biobank questionnaires, largely owing to the attention paid to ensure the acceptability of the invitation and questionnaire and the efficient use of reminders. Those who completed the MHQ appear to be better educated and have higher socio-economic employment status than those recruited into UK Biobank overall, and the UK population. Despite this, we found that rates of self-report diagnoses were similar to population estimates from the Health Survey England. The patterns of association between disorders and demographics were also broadly as predicted by previous research, which adds to the face validity of the questionnaire. For example, depression and anxiety were more common in women, while addiction and alcohol misuse were more common in men, and all disorders were less common in respondents older than 65 years. The decrease in prevalence of lifetime disorder with increasing age has been previously noted in cross-sectional studies, although the causes and implications are not clearly understood[21, 22].

The 'healthy volunteer' selection bias within the UK Biobank has been previously explored[23]. The impact of selection biases on disease prevalence are likely to be particularly strong for mental disorders, where disorder status or symptoms may influence participation in research,[24, 25] and non-participation has also been associated with many risk factors for these disorders, including polygenic risk.[26] Therefore, the results of the MHQ should not be used to provide prevalence estimates. However, the pattern of the measured risk factors among the participants with mental disorders in the MHQ, including neuroticism, trauma, loneliness and housing tenure, was in accordance with established literature, supporting the use of the data to study the relationships between exposures and outcomes. Previous work on health surveys with selection bias due to non-participation, including UK Biobank, have indicated that while they can be used to give estimates of association,[11, 24, 27] bias may occur in some cases.[28, 29] For example, the relative underparticipation of unskilled workers in the MHQ (around 21% of expected) could mask an association with a variable that was related to unskilled work.

Strengths and Limitations

We developed a questionnaire through a consensus approach with clear aims of capturing enough data to characterise participants as having a lifetime history of depression and other phenotypes. Validated instruments were used where possible. The consortium working on the questionnaire included mental health researchers and members of the UK Biobank team working in collaboration to develop the optimum approach. The derived variables of likely categorical diagnoses will be added to the UK Biobank resource, facilitating those less familiar with mental health to use the results efficiently.

The 'healthy volunteer' effect may limit applications of the data. Due to restrictions of time and space, the questionnaire was limited in the topics it could cover. The focus of the questionnaire was on categorical diagnoses rather than dimensional traits, which will tend to confirm conventional ICD/DSM nosology of psychiatric disorder and may not suit some research[30]. In particular, tools were chosen that are based on DSM-IV disorders, which reflects current practice (for example NICE Guidelines on depression and anxiety use DSM IV definitions)[31, 32]. Of the disorders with operational classification, all would generalise to DSM-5, except post-traumatic stress disorder[33], and the concepts are valid for ICD-10 disorders, although the threshold of disorder may be different, e.g. depression is diagnosed with fewer symptoms in DSM than ICD[31]. The questionnaire was heavily reliant on participant report, which may be affected by stigma of reporting psychiatric symptoms, and tends to underestimate lifetime prevalence through forgetting or re-evaluating distant events[11, 21, 34]. We hope that some of these shortcomings can be addressed in the future by a more fine-grained analyses of the MHQ data, supplemented with other data from UK Biobank to create a richer picture of mental health in the cohort.

Conclusions

UK Biobank offers a unique opportunity to research common disorders in a well characterised longitudinal cohort of UK adults. A detailed mental health questionnaire has now been completed by 157,366 participants, including self-report, operationally defined lifetime disorder status, and detailed phenotype information on mood disorder. The proportion of cases and the patterns of participants experiencing symptoms and disorders was as expected despite a "healthy volunteer" selection bias. Future work on mental health phenotyping for UK Biobank will include validation of Hospital Episode Statistics for mental health diagnoses, validation of general practice records, and triangulation of health record and questionnaire data. Examples of existing projects utilising the UK Biobank MHQ can be seen in supplementary material appendix 3, with a searchable database of approved research (http://www.ukbiobank.ac.uk/approved-research/).

This study also demonstrates of the substantial burden of mental disorders. Given the known impact of mental health on physical health, mental health data should interest researchers from every biomedical specialty looking at associations with health and disease. This study suggests that UK Biobank could be a powerful tool for such studies, and since it is open to all *bona fide* health researchers for work in the public good, we hope this study will inspire both existing and new users of UK Biobank.

Acknowledgements:
We thank the staff and participants of UK Biobank, the PROTECT study and the SLaM Service Users Group for their participation.

Funding

This paper represents independent research funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London.

In addition, individual authors have declared the following funding:

MA is supported by a Wellcome Trust Strategic Award (Reference 10436/Z/14/Z)

BC is funded by the Scottish Executive Chief Scientist Office (DTF/14/03) and by The Dr Mortimer and Theresa Sackler Foundation.

EF is supported by the European Research Council (ERC) under the European Union's Seventh Framework Programme (FP7/2007-2013)/ERC grant agreement no: [324176].

LMH is supported by an NIHR Research Professorship (NIHR-RP-R3-12-011) in Women's Mental Health.

AJ is funded by the Farr Institute and HCRW (CA-04)

WL is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South West Peninsula.

AM is supported by a Wellcome Trust Strategic Award (Reference 10436/Z/14/Z)

DS receives funding from a Lister Institute Prize Fellowship (2016-2021)

SZ is supported by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, Department of Health, ERC, Scottish Government, UK Biobank or other funders or institutions.

Conflicts of interest:

All authors have completed an ICJME conflict of interest form.

GB reports grants from National Institute for Health Research during the conduct of the study; support from Illumina Ltd. and the European Commission outside the submitted work.

BC reports grants from the Scottish Executive Chief Scientist Office during the conduct of the study.

CS reports grants from MRC & Wellcome Trust, during the conduct of the study; and is the Chief Scientist for UK Biobank.

MH reports grants for IMI RADAR-CNS and personal fees as an expert witness outside the submitted work.

Other authors have nothing to declare.

REFERENCES

1. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Medicine*. 2015; **12**(3): e1001779.
2. Weissman MM, Brown AS, Talati A. Translational Epidemiology in Psychiatry: Linking Population to Clinical and Basic Sciences. *Arch Gen Psychiatry*. 2011; **68**(6): 600-8.
3. Bell V. Open science in mental health research. *Lancet Psychiatry*. 2017: 10.1016/S2215-0366(17)30244-4.
4. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. *Lancet*. 2007; **370**(9590): 859-77.
5. Newton JN, Briggs ADM, Murray CJL, Dicker D, Foreman KJ, Wang H, et al. Changes in health in England, with analysis by English regions and areas of deprivation, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2015; **386**(10010): 2257-74.
6. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet*. 2012; **380**(9836): 37-43.
7. Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and cardiovascular disease. *Am J Hypertens*. 2015; **28**(11): 1295-302.
8. Chang C-K, Hayes RD, Broadbent MTM, Hotopf M, Davies E, Møller H, et al. A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. *BMJ Open*. 2014; **4**(1).
9. Smith DJ, Nicholl BI, Cullen B, Martin D, Ul-Haq Z, Evans J, et al. Prevalence and characteristics of probable major depression and bipolar disorder within UK biobank: cross-sectional study of 172,751 participants. *PLoS One*. 2013; **8**(11): e75362.
10. Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustun TB. Age of onset of mental disorders: A review of recent literature. *Curr Opin Psychiatry*. 2007; **20**(4): 359-64.
11. Newson RS, Karlsson H, Tiemeier H. Epidemiological fallacies of modern psychiatric research. *Nord J Psychiatry*. 2011; **65**(4): 226-37.
12. Davis KA, Sudlow CL, Hotopf M. Can mental health diagnoses in administrative data be used for research? A systematic review of the accuracy of routinely collected diagnoses. *BMC Psychiatry*. 2016; **16**(1): 263.
13. Pitman A, Osborn DPJ, King MB. The use of internet-mediated cross-sectional studies in mental health research. *BJPsych Adv*. 2015; **21**(3): 175-84.
14. Bridges S. Health Survey for England 2014: Mental Health Problems. In: *HSE 2014* (ed Health and Social Care Information Centre). Office of National Statistics, 2015.
15. Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). *Int J Methods Psychiatr Res*. 1998; **7**(4): 171-85.
16. Robotham D, Wykes T, Rose D, Doughty L, Strange S, Neale J, et al. Service user and carer priorities in a Biomedical Research Centre for mental health. *Journal of Mental Health*. 2016; **25**(3): 185-8.
17. Wesnes KA, Brooker H, Ballard C, McCambridge L, Stenton R, Corbett A. Utility, reliability, sensitivity and validity of an online test system designed to monitor changes in cognitive function in clinical trials. *Int J Geriatr Psychiatry*. 2017: 10.1002/gps.4659.
18. Cerimele JM, Chwastiak LA, Dodson S, Katon WJ. The prevalence of bipolar disorder in general primary care samples: a systematic review. *Gen Hosp Psychiatry*. 2014; **36**(1): 19-25.
19. Carvalho AF, Takwoingi Y, Sales PMG, Soczynska JK, Köhler CA, Freitas TH, et al. Screening for bipolar spectrum disorders: a comprehensive meta-analysis of accuracy studies. *J Affect Disord*. 2015; **172**: 337-46.
20. Joint Health Surveys Unit. Health Survey for England 2014: Volume 2 Methods and Documentation (available at http://content.digital.nhs.uk/catalogue/PUB19295) In: *HSE 2014* (eds R Craig, E Fuller, J Mindell). Office of National Statistics 2015.

21. Streiner DL, Patten SB, Anthony JC, Cairney J. Has 'lifetime prevalence' reached the end of its life? An examination of the concept. *Int J Methods Psychiatr Res*. 2009; **18**(4): 221-8.
22. Kessler RC, Birnbaum HG, Shahly V, Bromet E, Hwang I, McLaughlin KA, et al. Age differences in the prevalence and co-morbidity of DSM-IV major depressive episodes: results from the WHO World Mental Health Survey Initiative. *Depress Anxiety*. 2010; **27**(4): 351-64.
23. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with the general population. *Am J Epidemiol*. 2017: 10.1093/aje/kwx246.
24. Knudsen AK, Hotopf M, Skogen JC, Øverland S, Mykletun A. The health status of nonparticipants in a population-based health study: The Hordaland Health Study. *Am J Epidemiol*. 2010; **172**(11): 1306-14.
25. Atherton K, Fuller E, Shepherd P, Strachan DP, Power C. Loss and representativeness in a biomedical survey at age 45 years: 1958 British birth cohort. *J Epidemiol Community Health*. 2008; **62**(3): 216-23.
26. Martin J, Tilling K, Hubbard L, Stergiakouli E, Thapar A, Davey Smith G, et al. Association of genetic risk for schizophrenia with nonparticipation over time in a population-based cohort study. *Am J Epidemiol*. 2016; **183**(12): 1149-58.
27. Macfarlane GJ, Beasley M, Smith BH, Jones GT, Macfarlane TV. Can large surveys conducted on highly selected populations provide valid information on the epidemiology of common health conditions? An analysis of UK Biobank data on musculoskeletal pain. *Br J Pain*. 2015; **9**(4): 203-12.
28. Hernan MA, Hernandez-Diaz S, Robins JM. A Structural Approach to Selection Bias. *Epidemiology*. 2004; **15**(5): 615-25.
29. Sperrin M, Candlish J, Badrick E, Renehan A, Buchan I. Collider bias is only a partial explanation for the obesity paradox. *Epidemiology*. 2016; **27**(4): 525-30.
30. Lilienfeld SO, Treadway MT. Clashing diagnostic approaches: DSM-ICD Versus RDoC. *Annu Rev Clin Psychol*. 2016; **12**(1): 435-63.
31. National Institute for Health and Clinical Excellence. Depression in adults: recognition and management. NICE Clinical Guideline CG90. 2009 (updated 2016).
32. National Institute for Health and Clinical Excellence. Generalised anxiety disorder and panic disorder in adults: management. NICE Clinical Guideline CG113. 2011.
33. American Psychiatric Association. Highlights of Changes from DSM-IV-TR to DSM-5: psychiatry.org, 2013.
34. Nevin RL. Low validity of self-report in identifying recent mental health diagnosis among US service members completing Pre-Deployment Health Assessment (PreDHA) and deployed to Afghanistan, 2007: a retrospective cohort study. *BMC Public Health*. 2009; **9**(1): 376.

Table 1

Self-reported previous physician diagnosis[a] (self-reported without physician diagnosis for addiction[b]).
NA = not reported. See also lettered table notes.

	UK Biobank MHQ responses (age 45-82y)		Health Survey for England (HSE) (age 45-84y)	
	N=157,366	% in sample	N=3,272	Prevalence (95% CI)
All psychotic disorders	723	0.5	11	0.3 (0.2-0.6)
• *Schizophrenia*	157	0.1	NA	
• *Any other type of psychosis or psychotic illness*	604	0.4	NA	
Depression	33424	21.2	679	20.8 (19.4-22.2)
Mania, hypomania, bipolar or manic-depression	837	0.5	13	0.4 (0.2-0.7)
Anxiety, nerves or generalized anxiety disorder[c]	22036	14.0	170	5.2 (4.5-6)
Panic attacks	8704	5.5	262	8.0 (7.1-9.0)
Agoraphobia	599	0.4	NA	
Social anxiety or social phobia	1962	1.2	NA	
Any other phobia (eg disabling fear of heights or spiders)	2153	1.4	27	0.8 (0.6-1.2)
Obsessive compulsive disorder (OCD)	982	0.6	11	0.3 (0.2-0.6)
A personality disorder	385	0.2	13	0.4 (0.2-0.7)
All eating disorders	1851	1.2	26	0.8 (0.5-1.2)
• *Anorexia nervosa*	891	0.6	NA	
• *Bulimia nervosa*	503	0.3	NA	
• *Psychological over-eating or binge-eating*	707	0.4	NA	
Autism, Asperger's or autistic spectrum disorder	223	0.1	NA	
Attention deficit or attention deficit and hyperactivity disorder (ADD/ADHD)	133	0.1	4	0.1 (0-0.3)
Any addiction or dependence	9386	6.0	NA	
• Alcohol or drug addiction[b]	5002	3.2	30	0.9 (0.6-1.3)
• *Physical alcohol dependence*	946	0.6	NA	

Summary				
None of above	103346	65.7	2,356	72.0 (70.4-73.5)
1+ above	54020	34.3	916	28.0 (26.5-29.6)
2+ above	19400	12.3	NA	

a) UK Biobank participants asked: "Have you been diagnosed with one or more of the following mental health problems by a professional, even if you don't have it currently? (tick all that apply): By professional we mean: any doctor, nurse or person with specialist training (such as a psychologist or therapist). Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis."
HSE participants asked to identify all the mental health conditions they had experienced, then asked whether they had been told by a doctor, psychiatrist or professional that they had it.
b) UK Biobank participants asked: "Have you been addicted to or dependent on one or more things, including substances (not cigarettes/coffee) or behaviours (such as gambling)?". HSE definition of addiction includes physician diagnosis.
c) HSE participants were asked about Generalised Anxiety Disorder, and not about anxiety and nerves more generically

Table 2: Comorbidity between operationally defined syndromes. Percentages refer to the proportion of participants with the row syndrome who also have column syndrome. See lettered table notes, and Appendix 2 for case definitions.

			Comorbidity						
		Overall Prevalence	**Depression[1]**	**Hypomania / mania[2]**	**Anxiety disorder[3]**	**Unusual experiences[4]**	**Self-harm**	**Alcohol use disorder[6]**	**PTSD[32a]**
	Total=	55570 (35%)	37434 (24%)	2396 (2%)	11111 (7%)	7803 (5%)	6872 (4%)	10911 (7%)	10064 (6%)
Lifetime history	**Depression[a]**	37434 (24%)		1550 (4%)	8444 (23%)	3649 (10%)	4240 (11%)	3405 (9%)	6373 (17%)
	Hypomania/mania[b]	2396 (2%)	1550 (65%)		778 (32%)	598 (25%)	453 (19%)	327 (14%)	657 (27%)
	Anxiety disorder (GAD)[c]	11111 (7%)	8444 (76%)	778 (7%)		1551 (14%)	1704 (15%)	1286 (12%)	3274 (29%)
	Unusual experiences[d]	7803 (5%)	3649 (47%)	598 (8%)	1551 (20%)		1225 (16%)	768 (10%)	1594 (20%)
	Self-harm[e]	6872 (4%)	4240 (62%)	453 (7%)	1704 (25%)	1225 (18%)		959 (14%)	1719 (25%)
Current	**Alcohol use disorder[f]**	10911 (7%)	3405 (31%)	327 (3%)	1286 (12%)	768 (7%)	959 (9%)		1360 (12%)
	PTSD[g]	10064 (6%)	6373 (63%)	657 (7%)	3274 (33%)	1594 (16%)	1719 (17%)	1360 (14%)	

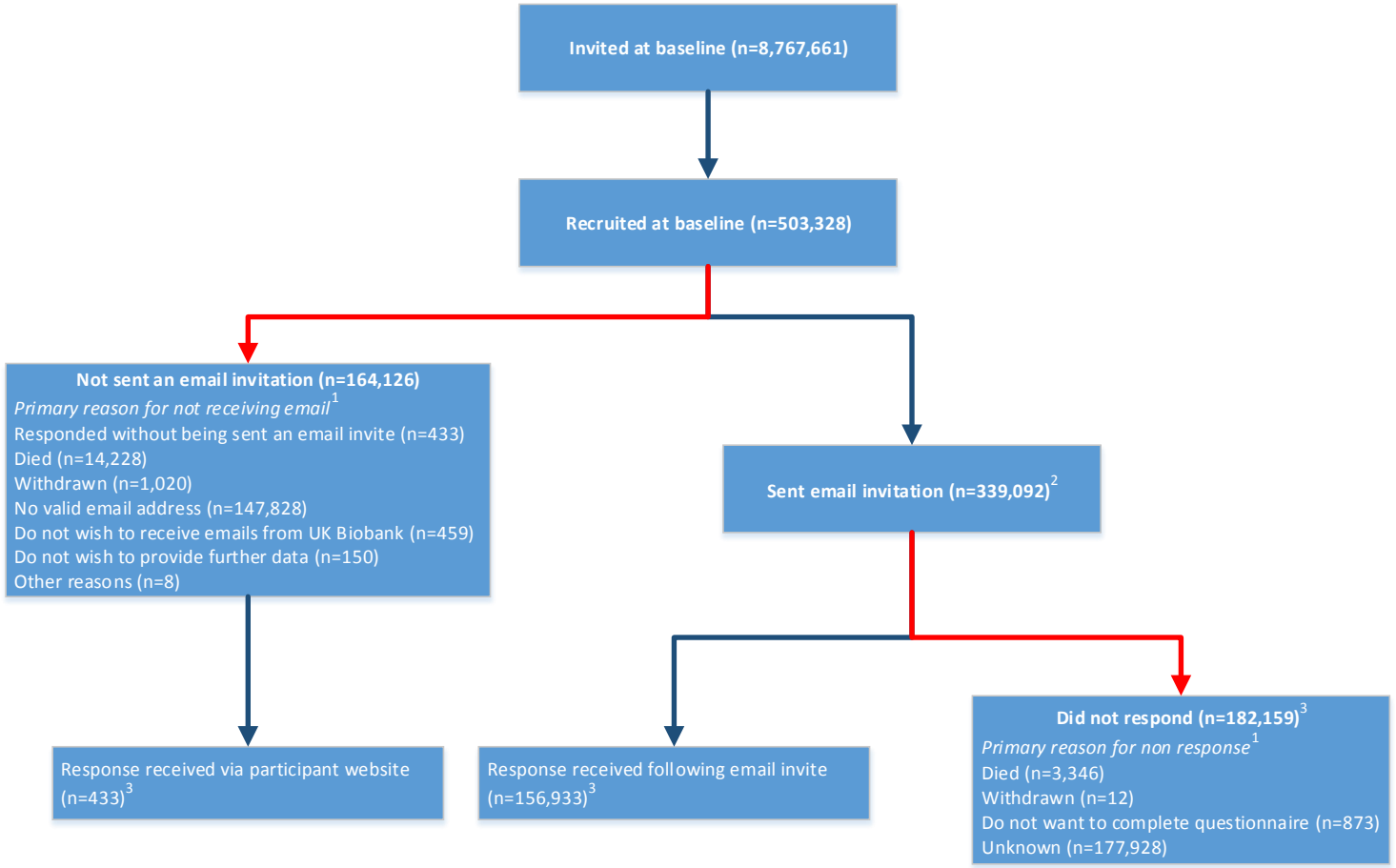
a) Criteria met for major depressive disorder on CIDI-SF lifetime
b) Criteria met for hypomania / mania lasting for at least one week
c) Criteria met for generalised anxiety disorder on CIDI-SF lifetime
d) Reported potential hallucination or delusion at any point in their life
e) Reported deliberate self-harm at some point in their life, asked to report self-harm "whether or not you meant to end your life"
f) Criteria met for moderate alcohol use disorder on AUDIT during the last year
g) Criteria met for post-traumatic stress disorder on PCL-6 in the last month

Table 3 Socioeconomic factors by status for lifetime occurrence (people may be included in more than one category). See lettered table notes, and Appendix 2 for full case definitions

		No "lifetime" criteria met[a] N=102,901	Depression[b] N=37,434	Bipolar type 1[c] N=931	Anxiety disorder (GAD)[b] N=11,111	Unusual experiences[d] N=7,803	Addiction[e] N=9,386
Personal Characteristics							
Age[f]	45-54	14364 (13%)	7145 (19%)	228 (24%)	2348 (21%)	1485 (19%)	2013 (21%)
	55-64	33307 (31%)	14809 (40%)	417 (45%)	4470 (40%)	2904 (37%)	3428 (37%)
	65-74	51705 (48%)	13739 (37%)	261 (28%)	3892 (35%)	2960 (38%)	3466 (37%)
	75+ (oldest is 82)	9376 (9%)	1741 (5%)	25 (3%)	401 (4%)	454 (6%)	479 (5%)
Gender	female	57556 (53%)	25815 (69%)	532 (57%)	7404 (67%)	4718 (60%)	4556 (49%)
Ethnicity	white	105072 (97%)	36297 (97%)	892 (96%)	10749 (97%)c	7503 (96%)	9037 (96%)
Townsend Deprivation Score[g]	most deprived (TDS ≥ +2)	11783 (11%)	5656 (15%)	201 (22%)	1856 (17%)	1426 (18%)	1941 (21%)
Highest qualification	degree	48700 (45%)	16939 (45%)	425 (46%)	5071 (46%)	3646 (47%)	4531 (48%)
Housing tenure	rent[h]	4162 (4%)	2906 (8%)	155 (17%)	1026 (9%)	854 (11%)	1109 (12%)
Known risk factors							
Neuroticism score[i]	mean (SD)	3.2 (2.8)	5.6 (3.3)	3.8 (3.1)	7.1 (3.3)	5.2 (3.5)	5.4 (3.5)
Adverse life experiences	childhood screen[j]	43913 (40%)	21144 (56%)	638 (69%)	6931 (62%)	4783 (61%)	5800 (62%)
	adult screen[k]	50226 (46%)	23893 (64%)	685 (74%)	7581 (68%)	4783 (61%)	6303 (67%)
	trauma exposure[l]	50771 (47%)	22166 (59%)	665 (71%)	6877 (62%)	5439 (70%)	6278 (67%)
Social connection	loneliness[i,m]	2976 (3%)	2367 (6%)	94 (10%)	971 (9%)	570 (7%)	669 (7%)
	social isolation[i]	7793 (7%)	3623 (10%)	126 (14%)	1173 (11%)	931 (12%)	1200 (13%)
Illness	longstanding illness, disability or infirmity[i]	26341 (24%)	13363 (36%)	503 (54%)	4581 (41%)	3242 (42%)	3588 (38%)
Health-behaviours							
Smoking status[i]	current	6235 (6%)	3638 (10%)	158 (17%)	1194 (11%)	837 (11%)	1916 (20%)
	former	36425 (33%)	13927 (37%)	323 (35%)	4009 (36%)	2943 (38%)	4893 (52%)
	never	65827 (61%)	19786 (53%)	448 (48%)	5883 (53%)	4003 (51%)	2547 (27%)
Cannabis use (lifetime)	daily	868 (1%)	914 (2%)	63 (7%)	346 (3%)	258 (3%)	867 (9%)
	ever, but not daily	19675 (18%)	9607 (26%)	299 (32%)	2818 (25%)	2312 (30%)	3487 (37%)
	never	88209 (81%)	26913 (72%)	569 (61%)	7947 (72%)	5233 (67%)	5032 (54%)
Physical activity[i]	moderate activity ≥ three times a week	93331 (86%)	31389 (84%)	751 (81%)	9253 (83%)	6522 (84%)	7796 (83%)

a) Criteria not met for depression, GAD, unusual experiences or addiction.
b) Criteria met for disorder on CIDI-SF lifetime
c) Criteria met for both lifetime depression and lifetime mania
d) Reported potential hallucination or delusion at any point in their life
e) Positively endorsed: “Have you been addicted to or dependent on one or more things, including substances (not cigarettes/coffee) or behaviours (such as gambling)?”
f) Age when mental health questionnaire released, derived from date of birth
g) Townsend material Deprivation Score is based on postcode areas
h) Collapsed from categories in table 2
i) From baseline assessment 2007-10
j) Criteria met for possible abuse or neglect on Childhood Trauma Screener
k) Criteria met for adverse situations as an adult: lack of confiding relationship, abusive relationships and money problems
l) Reports one or more of six situations that are known to be triggers for trauma-related disorders
m) There is some overlap between the adult screen and loneliness screen, which both ask about confiding relationships: adult screen includes lack of confiding relationship over the adult lifetime; loneliness includes lack of confiding relationship at the time of baseline assessment

Figure 1: Flowchart of UK Biobank (UKB) participants from invitation to completion of mental health questionnaire (MHQ). Invitations were based on NHS registration, age and location. Numbers correct for July 2017.



[1] Participants could have multiple reasons for not being sent an email, or for not responding. For the purposes of this flowchart, we have identified the most important reason why people were not sent an email.
[2] Emails were sent up to and including 24th July 2017. 110 email invites have been sent since this date – any resultant data are not included here.
[3] Cut off date for providing responses was 27th July 2017

Mental Health in UK Biobank – development, implementation and results from an online questionnaire completed by 157,366 participants. Davis, Coleman, et al.

Supplementary Material

Extra Tables and Figures

- Table SM1: The structure of the UK Biobank mental health questionnaire "thoughts and feelings"
- Table SM2 Characteristics of the participants who completed the MHQ questionnaire, compared to the whole UKB cohort at baseline, and to the UK population.
- Table SM3: Prevalence of operationally defined syndromes by gender. See lettered table notes, and Appendix 2 for full case definitions
- Figure SM1: Proportion of respondents positive for one or more of depression (and bipolar disorder), anxiety disorder (GAD), unusual experiences and addiction according to lifetime diagnostic criteria. By age and gender
- References for tables

Mood disorder

Appendix 1: Members of the UK Biobank Mental Health Consortium (January 2015)

Appendix 2: Case-control Definitions

Appendix 3: UK Biobank Approved Research

Appendix 4: Output for tables

- Table 2
- Table 3
- Table 4
- Table 5
- Table 6

Appendix 5: STROBE Checklist

Appendix 6: UK Biobank Showcase Documentation

- Full questionnaire

Extra tables and figure

Table SM1: The structure of the UK Biobank mental health questionnaire "thoughts and feelings"

Domain/question topic	Purpose	Source/tool	Notes about source/tool
A. Screening questions	To screen for presence and absence of any mental health condition.	Devised by the study team	
B. Current Depression	Indicates likely presence / absence and severity of current depression.	Patient Health Questionnaire 9-question version (PHQ-9)[1]	Maps on to criteria for DSM-IV major depressive disorder. This includes repeating the four PHQ questions asked at the baseline assessment.
B. Lifetime Depression	Assess lifetime history of symptoms of depression to stratify into cases and controls for genomic and other studies.	CIDI-SF (Composite International Diagnostic Interview – Short Form)[2], depression module, lifetime version	Maps on to DSM-IV major depressive disorder. Lifetime version by Doug Levinson. Allows comparison with other cohorts in the international Psychiatric Genetics Consortium (PGC).
B. Lifetime manic symptoms	Identify symptoms that may indicate a bipolar affective disorder, in particular to distinguish from unipolar depression.	Devised by the study team based on CIDI questions	These questions were also included in the baseline assessment for the last one-third of UK Biobank participants[3]
C. Current anxiety disorder	Indicates likely presence / absence and severity of anxiety disorder.	Generalised Anxiety Disorder Questionnaire– 7 questions (GAD-7)[1]	A tool commonly used in research and clinical practice with PHQ-9. Maps on to DSM-IV generalised anxiety disorder, but is also raised in other anxiety disorders[1].
C. Lifetime anxiety disorder	Assess lifetime occurrence of anxiety disorder.	CIDI-SF[2], anxiety module, lifetime version	Maps on to DSM generalised anxiety disorder. Lifetime version by Doug Levinson. Allows comparison with other cohorts in the PGC.
D. Addictions	Assess of a variety of addictions, past and current, through prompted self-report.	Devised by the study team	Common addictions were identified from the literature: alcohol, sedatives and painkillers, illicit drugs, and behaviours such as gambling
E. Alcohol Use	Comprehensive assessment of patterns in alcohol use, with a view to defining misuse.	Alcohol Use Disorders Identification Test (AUDIT)[4]	Developed by the WHO and extensively used and studied for alcohol use disorders, including hazardous, harmful and dependent drinking.
E. Cannabis Use	Identify cannabis use and pattern of use.	Devised by the study team	Two questions: times used and frequency used when using
F. Unusual experiences	Assess experience of phenomena that may be markers of psychosis.	CIDI, psychosis module, lifetime version, abridged[5]	The CIDI lifetime version is a World Health Organisation (WHO) instrument for mental health surveys. The CIDI questions were adapted for self-report and reduced in number to as few

			questions as possible to tap into this theme, while making it possible to compare with the World Mental Health Surveys.
G. Adverse events in childhood	Identify abuse and other adverse events in childhood.	Childhood Trauma Screener – 5 item (CTS-5)[6]	This is the short version of the Childhood Trauma Questionnaire, designed for adults to rate adverse events that may have happened in childhood[7].
G. Adverse events in adult life	Identify domestic abuse and other adverse events in adult life, and lifetime trauma	Devised by the study team, based on existing questions	Using the same structure as the CTS, the questions were adapted from the national crime survey questions to identify victims of crime and adult domestic violence[8]. A short checklist of possible catastrophic trauma was also included[9]
G. Post-traumatic stress disorder	Assess the occurrence of post-traumatic stress disorder.	Post-traumatic stress disorder Check List – civilian Short version (PCL-6)[10]	Maps onto the DSM-IV criteria and is well-validated. Does not require endorsement of specific items on the trauma checklist
H. Self-harm and suicidal thoughts	Assess self-harm and suicidal thoughts and associated outcomes.	Devised by the study team	There were no instruments that were considered adequate, especially in terms of distinguishing between self-harm without suicidal intent and suicide attempts. The working group devised a set of questions, working with service users group on acceptability.
J. Subjective wellbeing	Included in response to feedback for the service user group	Devised by the study team, based on existing questions	Measures of wellbeing, two euthymic ('positive emotion') questions UKB baseline and one eudemonic ('meaning') question from the WHO-Quality Of Life (WHOQOL) [11].
K. Free-text box	To enable participants to add any further information about their mental health status. Included in response to piloting		In response to piloting feedback, we included a text box for the participant to elaborate on their answers and to increase the participants' confidence in the questionnaire.

Table SM2 Characteristics of the participants who completed the MHQ questionnaire, compared to the whole UKB cohort at baseline, and to the UK population.
Characteristics at baseline unless stated
NA = missing, not stated or not available.
See lettered table notes, and Appendix 2 for full case definitions. Numbers in superscript are references.

		UKB baseline[a] N=501,730	UKB MHQ[b] N=157,366	Illustrative population data	Population data details[c]
Personal Characteristics					
Age[d]	45-54	15%	15%	36%	Census UK 2011[12], as proportion of people aged 45-82
	55-64	30%	33%	30%	
	65-74	44%	45%	22%	
	75+ (oldest is 82)	11%	8%	12%	
Gender	male	46%	43%	48%	Census EWS 2001[13] age 40-69
	female	54%	57%	52%	
Ethnicity	white	94%	97%	95%	Census EWS 2001[13] age 40-69
	black	2%	1%	2%	
	asian (indian sub-continent)	2%	1%	3%	
	mixed	1%	1%	<0.5%	
	chinese	<0.5%	<0.5%	<0.5%	
	other	1%	1%	1%	
	NA	1%	<0.5%	NA	
Migrant to UK[e]		9%	7%	NA	
Townsend Deprivation Score (TDS)[f]	most deprived (TDS ≥ +2)	16%	12%	30%	TDS of people invited to take part in UK Biobank, as reported in Fry et al[14]
	middle (TDS -2 to +1.99)	32%	31%	34%	
	least deprived (TDS < -2)	52%	56%	30%	
Highest qualification	none	17%	7%	38%	Census EWS 2011[12] age 50+
	other (including vocational)	5%	5%	12%	
	Secondary school equivalent	33%	29%	21%	
	A-level or equivalent	11%	13%	7%	
	degree	32%	45%	23%	
	NA	2%	1%	NA	
SOC job code[g]	Higher managerial, administrative and professional	47%	60%	35%	

	Intermediate occupations and small employers	11%	8%	21%	Census EW 2001[13] age 45-64 (combined current occupation and former occupation for not working)
	Routine and manual occupations	6%	4%	19%	
	NA	35%	29%	17%	
Household					
Own or rent	own outright	52%	55%	41%	Census EW 2001[13] age 50-64
	own with mortgage	37%	38%	40%	
	rent – social	6%	3%	13%	
	rent – private	3%	2%	5%	
	other	2%	2%	2%	
Average household income	less than £18,000	21%	12%	NA	
	18-30,000	24%	21%	NA	
	31-52,000	24%	26%	NA	
	52-100,000	18%	23%	NA	
	>£100,000	5%	7%	NA	
	Not stated	15%	10%	NA	
Live with husband, wife or partner		76%	75%	77%	Census EW 2001[13] age 50-64
Health and health-behaviours					
Smoking status	current	11%	7%	19%	HSE 2008 age 45-64, as reported in Fry et al[14] Number out of 4647
	former	49%	35%	31%	
	never	40%	57%	49%	
Felt depressed in last two weeks (baseline)	"Not at all"	73%	77%	NA	
	"Several days" or more	23%	20%	NA	
	NA	5%	3%	NA	
Report longstanding illness, disability or infirmity	Yes	32%	28%	37%	Census EW 2001[13] age 50-64
	No	66%	70%	63%	
	NA	3%	2%	0%	
Self-report physician diagnosis	Diabetes	5%	3%	5%	HSE 2009 age 45-64[15] Number out of 1395
	Cancer	8%	7%	NA	

a) The whole UK Biobank cohort for whom information was available on 8 August 2017 (including deceased)

b) The UK Biobank participants who completed the questionnaire in time for the data release on 8 August 2017

c) Census data from 2001 or 2011 as available for UK, EWS = England, Wales and Scotland, Eng. = England, EW = England and Wales. Where census data unavailable Health Survey for England (HSE) is used, which is a survey of around 10,000 people that through sampling and weighting of data, attempts to derive data that is representative of the population in England.

d) Age when mental health questionnaire released, derived from date of birth
e) Not born in UK
f) Townsend material Deprivation Score is based on postcode areas, derived from the census data for those areas in the domains of access to a car, overcrowding of housing, lack of owner-occupation and unemployment. The tertiles are based on those used in the Fry et al. paper on socioeconomic features of UK Biobank
g) Cascot job codes, reported in nine classes in UK Biobank, arranged into three categories. UK Biobank has both directly coded and derived job codes, and we used both, but there remained significant proportion of participants with no job code. NA also includes 'never worked'.

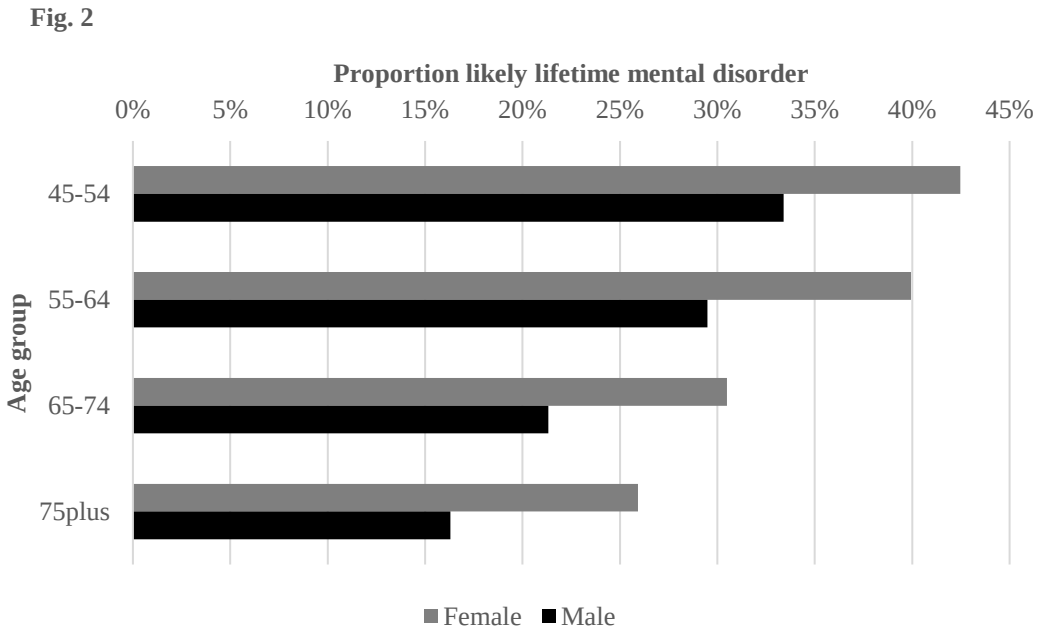
.

Table SM3**:** Prevalence of operationally defined syndromes by gender. See lettered table notes, and Appendix 2 for full case definitions.

		Total (n=157,366)	Female (n=89,101)	Male (n=68,265)
Lifetime history	**Depression**[a]	37434 (24%)	25815 (29%)	11619 (17%)
	Hypomania/mania[b]	2396 (2%)	1288 (1%)	1108 (2%)
	Lifetime anxiety disorder (GAD)[c]	11111 (7%)	7404 (8%)	3707 (5%)
	Unusual experience[d]	7803 (5%)	4718 (5%)	3085 (5%)
	Self-harm[e]	6872 (4%)	4770 (5%)	2102 (3%)
Recent or current	**Alcohol use disorder**[f]	10911 (7%)	4063 (5%)	6848 (10%)
	PTSD[g]	10064 (6%)	6709 (8%)	3355 (5%)
Overall	**None of above**	101796 (65%)	54280 (61%)	47516 (70%)
	1+ of above	55570 (35%)	34821 (39%)	20749 (30%)

a) Criteria met for major depressive disorder on CIDI-SF lifetime
b) Criteria met for hypomania / mania lasting for at least one week in their life
c) Criteria met for generalised anxiety disorder on CIDI-SF lifetime
d) Report potential hallucincation or delusion at any point in their life
e) Report deliberate self-harm at some point in their life, whether or not they meant to end their life
f) Criteria met for moderate alcohol use disorder on AUDIT during the last year
g) Criteria met for post-traumatic stress disorder on PCL-6 in the last month

Figure SM1: Proportion of respondents positive for one or more of depression (and bipolar disorder), anxiety disorder (GAD), unusual experiences and addiction according to lifetime diagnostic criteria. By age and gender.



Data for figure (not for publication)

		n	1+ lifetime disorder	1+ lifetime disorder (%)
Female	45-54	14051	5968	42%
	55-64	31307	12504	40%
	65-74	37908	11560	30%
	75plus	5835	1513	26%
Male	45-54	9431	3150	33%
	55-64	20568	6064	29%
	65-74	32228	6871	21%
	75plus	6038	984	16%

References for extra tables

1. Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. *General Hospital Psychiatry*. 2010; **32**(4): 345-59.
2. Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). *Int J Methods Psychiatr Res*. 1998; **7**(4): 171-85.
3. Smith DJ, Nicholl BI, Cullen B, Martin D, Ul-Haq Z, Evans J, et al. Prevalence and characteristics of probable major depression and bipolar disorder within UK biobank: cross-sectional study of 172,751 participants. *PLoS One*. 2013; **8**(11): e75362.
4. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. *Alcoholism: Clinical and Experimental Research*. 2007; **31**(2): 185-99.
5. McGrath JJ, Saha S, Al-Hamzawi A, et al. Psychotic experiences in the general population: a cross-national analysis based on 31 261 respondents from 18 countries. JAMA psychiatry 2015; 72(7): 697-705.
6. Glaesmer H, Schulz A, Häuser W, Freyberger HJ, Brähler E, Grabe H-J. [The childhood trauma screener (CTS)-development and validation of cut-off-scores for classificatory diagnostics]. *Psychiatrische Praxis*. 2013; **40**(4): 220-6.
7. Walker EA, Gelfand A, Katon WJ, Koss MP, Von Korff M, Bernstein D, et al. Adult health status of women with histories of childhood abuse and neglect. *Am J Med*. 1999; **107**(4): 332-9.
8. Khalifeh H, Oram S, Trevillion K, Johnson S, Howard LM. Recent intimate partner violence among people with chronic mental illness: findings from a national cross-sectional survey. *The British Journal of Psychiatry*. 2015; **207**(3): 207-12.
9. Frissa S, Hatch SL, Fear NT, Dorrington S, Goodwin L, Hotopf M. Challenges in the retrospective assessment of trauma: comparing a checklist approach to a single item trauma experience screening question. *BMC psychiatry*. 2016; **16**(1): 20.
10. Wilkins KC, Lang AJ, Norman SB. Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. *Depression and anxiety*. 2011; **28**(7): 596-606.
11. Forgeard MJ, Jayawickreme E, Kern ML, Seligman ME. Doing the right thing: Measuring wellbeing for public policy. *International Journal of Wellbeing*. 2011; **1**(1).
12. Office for National Statistics, National Records of Scotland, Northern Ireland Statistics and Research Agency. 2011 Census aggregate data. UK Data Service. This information is licensed under the terms of the Open Government Licence [http://www.nationalarchives.gov.uk/doc/open-government-licence/version/2]. 2017.
13. Office for National Statistics. 2001 Census aggregate data. UK Data Service.: 2011
14. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with the general population. *Am J Epidemiol*. 2017: 10.1093/aje/kwx246.
15. National Centre for Social Research, University College London. Health Survey for England 2009. UK Data Archive, 2015.

Supplementary material: Mood disorder

Using data on participants' history of depression and hypomania/mania, we divided the cohort according to five likely mood disorder categories as shown in Figure MD1. To be classified as having met DSM criteria for depression, participant needed to have five symptoms including depressed mood and/or anhedonia, for most of the time for two weeks. To be classified as having hypomanic / manic symptoms, participants needed to have four symptoms including high elevated mood or five symptoms with irritable mood. Subthreshold depression was used when participants had depressed mood and/or anhedonia most of the time for two weeks, but didn't have five symptoms in total; also, if they had a diagnosis of depression but had not met diagnostic criteria or if they appeared to have current depression on the PHQ despite not meeting diagnostic criteria.

While we would expect most participants with DSM IV bipolar affective disorder type I to be categorised as such, bipolar disorder without depression (i.e. recurrent mania) will be included in the "no depression" category. Participants who have experienced less disruptive symptoms of hypomania (including many with DSM IV bipolar affective disorder type II) will be included in the single depression or recurrent depression categories.

Table MD1 shows the socio-demographic and risk factors by likely mood disorder categories. Respondents with unipolar depression appear to be more likely to be female, an association not shared with those with bipolar disorder. Participants with likely bipolar disorder were younger, and resided in more deprived areas on average. Respondents with subthreshold depressive symptoms or any likely mood disorder group reported more lifetime adverse events, but these were highest for those respondents with bipolar disorder. There are also elevated rates of neuroticism, loneliness and longstanding illness or disability among subthreshold, unipolar depression and bipolar disorder.

Table MD2 shows that the other operationally defined syndromes are more common amongst respondents with a likely mood disorder. Table MD3 reports current mental state of the participants from the average score on the scales included in the MHQ, again split by likely mood disorder, which shows some variation between the groups. Notably, wellbeing appears to be affected by depressive symptoms, whether or not reaching diagnostic criteria.

Figure MD1: Subclassification of mood disorder

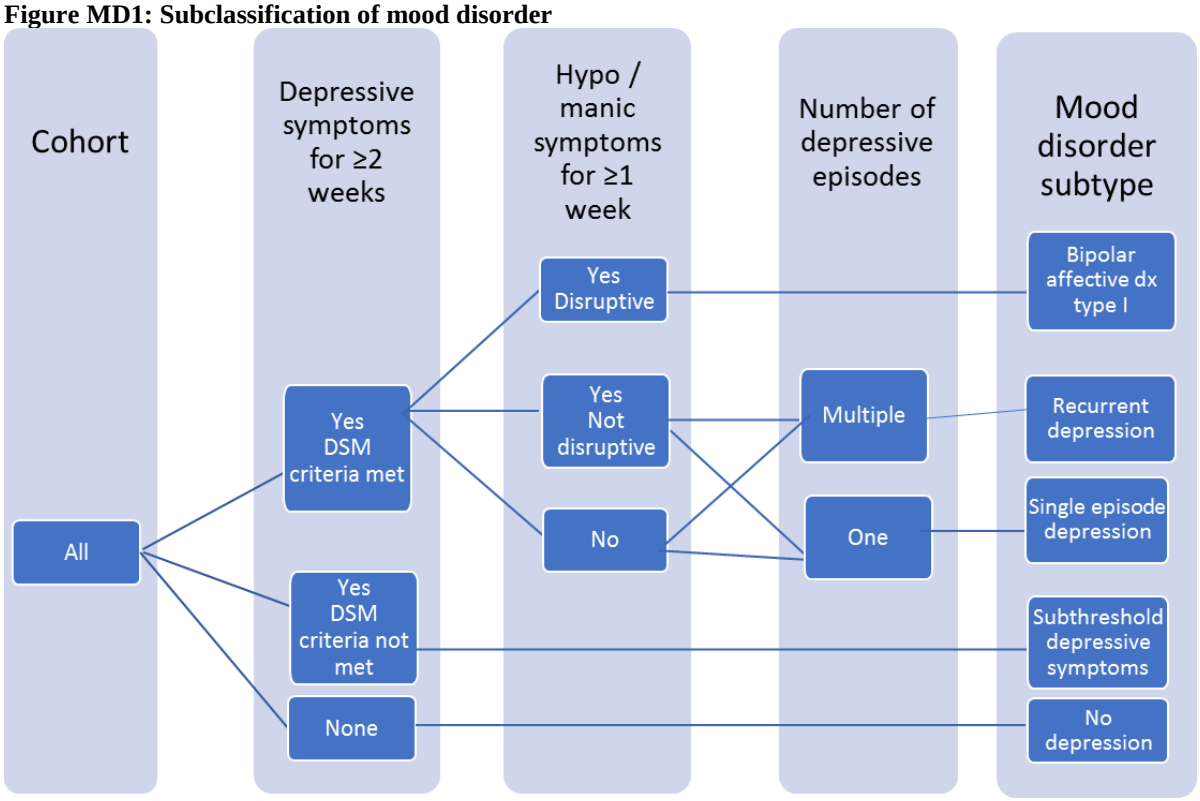


Table MD1

Socioeconomic factors by screening status for lifetime occurrence of mood disorders broken down into exclusive categories. See figure s1 for categorisation details.

		No depression[a] (n=88,650)	Subthreshold depressive symptoms[b] (n=27,207)	Lifetime depression[c], single episode (n=14,683)	Lifetime depression[c], recurrent[d] (n=21,187)	Bipolar affective disorder type 1[e] (n=931)
Personal Characteristics						
Age[f]	45-54	11332 (13%)	4298 (16%)	2454 (17%)	4334 (20%)	228 (24%)
	55-64	26755 (30%)	8894 (33%)	5450 (37%)	8709 (41%)	417 (45%)
	65-74	42800 (48%)	11972 (44%)	5939 (40%)	7297 (34%)	261 (28%)
	75+ (oldest is 82)	7763 (9%)	2043 (8%)	840 (6%)	847 (4%)	25 (3%)
Gender	female	44831 (51%)	16105 (59%)	9902 (67%)	15000 (71%)	532 (57%)
Ethnicity	white	85731 (97%)	26185 (96%)	14299 (97%)	20509 (97%)	892 (96%)
Townsend Deprivation Score[g]	most deprived (TDS ≥ +2)	9204 (10%)	3927 (14%)	1800 (12%)	3518 (17%)	201 (22%)
Highest qualification	degree	40597 (46%)	11648 (43%)	6582 (45%)	9665 (46%)	425 (46%)
Housing tenure	rent[h]	3024 (3%)	1825 (7%)	796 (5%)	1869 (9%)	155 (17%)
Risk factors						
Neuroticism score[i]	mean (SD)	2.8 (2.6)	5.0 (3.2)	4.6 (3.3)	6.2 (3.3)	3.8 (3.1)
Adverse life experiences	childhood screen[j]	34223 (39%)	13907 (51%)	7283 (50%)	12823 (61%)	638 (69%)
	adult screen[k]	38802 (44%)	15962 (59%)	8406 (57%)	14361 (68%)	685 (74%)
	trauma exposure[l]	40761 (46%)	14675 (54%)	8052 (55%)	13049 (62%)	665 (71%)
Social connection[i,m]	loneliness	1704 (2%)	1715 (6%)	621 (4%)	1602 (8%)	94 (10%)
	social isolation	5927 (7%)	2651 (10%)	1287 (9%)	2336 (11%)	126 (14%)
Illness[i]	longstanding illness, disability or infirmity	19846 (22%)	9046 (33%)	4443 (30%)	8072 (38%)	503 (54%)
Health-behaviours						
Smoking status[i]	current	5077 (6%)	2334 (9%)	1223 (8%)	2171 (10%)	158 (17%)
	former	29909 (34%)	10006 (37%)	5432 (37%)	7915 (37%)	323 (35%)
	never	53450 (60%)	14796 (54%)	7994 (54%)	11058 (52%)	448 (48%)
Cannabis use	ever daily	838 (1%)	500 (2%)	246 (2%)	584 (3%)	63 (7%)
	ever, but not daily	16129 (18%)	5957 (22%)	3345 (23%)	5778 (27%)	299 (32%)
	never	71683 (81%)	20750 (76%)	11092 (76%)	14825 (70%)	569 (61%)
Physical activity[i]	moderate activity ≥3 times a week	76721 (87%)	22630 (83%)	12465 (85%)	17666 (83%)	751 (81%)

a) Does not meet criteria for major depressive disorder or subthreshold depressive symptoms
b) Does not meet criteria for major depressive disorder, but features suggestive of increased symptoms compared to general population
c) Criteria met for major depressive disorder on CIDI-SF lifetime
d) Reports more than one episode or "too many to recall"
e) Criteria met for major depressive disorder and mania
f) Age when mental health questionnaire released, derived from date of birth
g) Townsend material Deprivation Score is based on postcode areas[14]
h) Collapsed from categories in table 2
i) From baseline assessment 2007-10
j) Criteria met for possible abuse or neglect on Childhood Trauma Screener
k) Criteria met for stressful situations, including abusive relationships and money problems, as an adult
l) Reports one or more of six situations known to be triggers for trauma-related mental disorders

m) There is some overlap between the adult adverse life experiences screen and loneliness screen, which both ask about confiding relationships: adult screen includes lack of confiding relationship over the adult lifetime; loneliness includes lack of confiding relationship at the time of baseline assessment

Table MD2

The occurrence of other psychiatric disorders in people positive for categories of mood disorder (comorbidities). See lettered table notes, and Appendix 2 for full case definitions

	No depression[a] (n=88,650)	Subthreshold depressive symptoms[b] (n=27,207)	Lifetime depression[c], single episode (n=14,683)	Lifetime depression[c], recurrent[d] (n=21,187)	Bipolar affective disorder type 1[e] (n=931)
Lifetime anxiety disorder (GAD)[f] (n=11,111)	746 (1%)	1806 (7%)	1770 (12%)	6035 (28%)	449 (48%)
Current alcohol use disorder[g] (n=10,911)	4781 (5%)	2384 (9%)	1014 (7%)	2172 (10%)	150 (16%)
Current PTSD[h] (n=10,064)	705 (1%)	2776 (10%)	1122 (8%)	4684 (22%)	366 (39%)
Lifetime unusual experiences[i] (n=7,803)	2314 (3%)	1642 (6%)	904 (6%)	2263 (11%)	329 (35%)
Lifetime hypomania/mania[j] (n=2,396)	351 (<0.5%)	454 (2%)	123 (1%)	496 (2%)	931 (100%)
Overall					
None (n=131,940)	82739 (93%)	21972 (81%)	11336 (77%)	12095 (57%)	0 (0%)
At least one (n=25,422)	5911 (7%)	5235 (19%)	3347 (23%)	9092 (43%)	931 (100%)
Multiple (n=4,447)	340 (<0.5%)	763 (3%)	445 (3%)	2067 (10%)	678 (73%)

a) Does not meet criteria for major depressive disorder or subthreshold depressive symptoms
b) Does not meet criteria for major depressive disorder, but features suggestive of increased symptoms compared to general population
c) Criteria met for major depressive disorder on CIDI-SF lifetime
d) Reports more than one episode or "too many to recall"
e) Criteria met for major depressive disorder and mania
f) Criteria met for generalised anxiety disorder on CIDI-SF lifetime
g) Criteria met for moderate alcohol use disorder on AUDIT during the last year
h) Criteria met for post-traumatic stress disorder on PCL-6 in the last month
i) Reported hallucincation and/or delusion at any point in their life
j) Criteria met for hypomania / mania lasting for at least one week

Table MD3

The current mental status by scores of symptoms of current disorder for categories of mood disorder. See lettered table notes, and Appendix 2 for full case definitions.

Mean (SD) Median	No depression[a] (n=88,650)	Subthreshold depressive symptoms[b] (n=27,207)	Lifetime depression[c], single episode (n=14,683)	Lifetime depression[c], recurrent[d] (n=21,187)	Bipolar affective disorder type 1[e] (n=931)
Depression score PHQ-9 scale 0-36, high = more depressed	1.1 (1.2) 1[f]	5.1 (4.3) 5	3.1 (3.6) 2	5.9 (5.5) 4	7.9 (7.0) 6
Anxiety score GAD-7 scale 0-28, high = more anxious	1.0 (1.8) 0	3.5 (4.0) 2	2.5 (3.5) 1	4.7 (4.9) 4	6.2 (6.1) 5
Alcohol use disorder score AUDIT scale 0-42, high = more hazardous	2.0 (2.8) 1	2.4 (3.5) 1	2.0 (3.2) 1	2.6 (3.9) 1	3.4 (4.9) 1
Wellbeing score scale 3-22, high = better wellbeing	13.3 (1.6) 13	11.9 (2.1) 12	12.5 (2.0) 13	11.4 (2.3) 12	11.0 (2.7) 11

a) Does not meet criteria for major depressive disorder or subthreshold depressive symptoms
b) Does not meet criteria for major depressive disorder, but features suggestive of increased symptoms compared to general population
c) Criteria met for major depressive disorder on CIDI-SF lifetime
d) Reports more than one episode or "too many to recall"
e) Criteria met for major depressive disorder and mania
f) A PHQ-9 score above 5 would exclude the participant from the "No depression" category

Appendix 1:
Members of the UK Biobank Mental Health Consortium (January 2015).

Chair: Matthew Hotopf, Psychological Medicine and SLaM/Institute of Psychiatry, Psychology and Neuroscience Biomedical Research Centre, Kings College London

Steering Group Members

· Gerome Breen, MRC Social, Genetic & Developmental Psychiatry Centre, Kings College London
· Katrina Davis, Research Assistant to Matthew Hotopf
· Elaine Fox, Oxford Centre for Emotions and Affective Neuroscience, Department of Experimental Psychology, University of Oxford
· Louise Howard, Section of Women's Mental Health, Health Service and Population Research, Kings College London
· Ann John, College of Medicine, Swansea University Medical School and National Centre for Mental Health
· Rose McCabe, Clinical Communication and Mental Health, University of Exeter
· Andrew McIntosh, Division of Psychiatry, University of Edinburgh and Scottish Mental Health Research Network
· Daniel Smith, Institute of Health and Wellbeing, University of Glasgow
· Stan Zammit, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University

Members

· Naomi Allen, University of Oxford and UK Biobank
· David Batty, Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh and University College London
· Cyrus Cooper, MRC Lifecourse Epidemiology Unit, University of Southampton
· Tim Croudace, Centre for Health and Population Sciences, University of York
· Ian Deary, Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh
· Christopher Dickens, Institute of Health Service Research, University of Exeter
· Klaus Ebmeier, Division of Psychiatry, University of Oxford
· Seena Fazel, Division of Psychiatry, University of Oxford
· Robin Flaig, Assistant to Cathie Sudlow for UK Biobank
· Jonathon Flint, Wellcome Trust Centre for Human Genetics, University of Oxford
· John Gallacher, University of Oxford and MRC Dementias Platform UK
· Simon Gilbody, Centre for Health and Population Sciences, University of York
· Hazel Inskip, MRC Lifecourse Epidemiology Unit, University of Southampton
· Tony Kendrick, Department of Primary Care, University of Southampton
· David Kingdon, University of Southampton and Mental Health Foundation
· William Lee, Plymouth University Peninsula Schools of Medicine and Dentistry & Devon Partnership NHST.
· Glyn Lewis, Clinical Trials and Applied Epidemiology in Psychiatry, University College London
· Donald Lyall, Institute of Health and Wellbeing, University of Glasgow
· Donald MacIntyre, Division of Psychiatry, University of Edinburgh
· Susan McAndrew, Mental Health and Wellbeing Unit, University of Salford
· Peter McGuffin, MRC Social, Genetic & Developmental Psychiatry Centre, Kings College London
· Irwin Nazareth, Primary Care and Public Health, University College London
· Barbara Nicholl, Institute of Health and Wellbeing, University of Glasgow
· Michael O'Donovan, Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University
· Jolanta Opacka-Juffry, Health Sciences Research Unit, Rohampton University
· David Osborn, Division of Psychiatry, University College London
· Michael Owen, Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University
· Carmine Pariante, Department of Psychological Medicine, Kings College London
· Marcus Richards, Population Health Sciences, University College London
· Theresa Rushe, Department of Psychology, Queens University Belfast
· Valerie Shanks-Pepper, Medical Directorate, NHS England
· Stephen Stansfeld, Centre for Psychiatry, Queen Mary University of London
· Geraldine Strathdee, University College London and NHS England
· Cathie Sudlow, University of Edinburgh and UK Biobank
· Elizabeth Tunbridge, Department of Psychiatry, University of Oxford

· Scott Weich, Mental Health and Wellbeing, University of Warwick
· Peter Woodruff, Academic Clinical Psychiatry, University of Sheffield
· Allan Young, Department of Psychological Medicine, Kings College London

International Contributors
· Brenda Penninx, Professor of Psychiatric Epidemiology, VU University Amsterdam, NL
· Douglas Levinson, Professor of Psychiatry, Stanford University, USA
· Kenneth Kendler, Professor and Eminent Scholar Psychiatry, Virginia Commonwealth University, USA
· Hans Grabe, Professor in the Department of Psychiatry and Psychotherapy, Greifswald University, GL
John McGrath, Niels Bohr Professor, National Centre for Register-based Research, Aarhus University, Denmark & University of Queensland, AUS

Appendix 2: Case Criteria Derived from the UK Biobank Mental Health Questionnaire

Tables refer to the tables in results section and supplementary material of Davis et al. *Mental Health in UK Biobank – development, implementation and results from an online questionnaire completed by 157,366 participants.*

Control definitions are fairly stringent, creating control groups for applications where higher certainty that control groups do not contain cases. For the above paper, non-caseness was used rather than the control definitions below, and this may be preferred for many purposes.

Tables	**Disorder / Exposure**	**Rule in English**	**Fields and codes**	**Notes and references**
Mood disorder				
4	Depression	**Case: Depression ever.**		
5 6		At least one core symptom of depression, most or all of the day on most or all days for a two week period, with at least five depressive symptoms that represent a change from usual occurring over the same time-scale, with some or a lot of impairment.	Persistent sadness (20446) = Yes OR Loss of interest (20441) = Yes AND How much of day (20436) = Most of day or All day long AND Did you feel this way (20439) = Almost every day or Every day AND Impairment (20440) = Somewhat or A lot AND Total number of symptoms endorsed (core and others) >= 5 • Persistent sadness (core) 20446; Loss of interest (core) 20441; Tired or low energy 20449; Gain or loss of weight 20536 = Gain, Loss or Gain and loss; Sleep change 20532; Trouble concentrating 20435; Feeling worthless 20450; Thinking about death 20437	CIDI-SF (Composite International Diagnostic Interview – Short Form), depression module, lifetime version. Scored based on DSM definition of major depressive disorder *Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). Int J Methods Psychiatr Res. 1998;7(4):171-85.*
s1 s2 s3	Depression	**Case: Subthreshold depressive symptoms ever.** Does not meet diagnostic criteria for depression on the CIDI, but has at least one of: (i) endorses persistent depression or anhedonia on CIDI; (ii) PHQ9 (current depressive symptoms) is over threshold for mild depression; (iii) reports clinician diagnosis of depression	NOT Case {depression ever} AND ((reported diagnosis of depression 20544 or 20002) OR Core symptoms from above OR PHQ score >5)	Case plus control plus subthreshold should include all participants with valid responses Subthreshold symptoms may have clinical significance *National Institute for Health and Clinical Excellence. Depression in adults: recognition and management. NICE Clinical Guideline CG90 (available at*

				https://www.nice.org.uk/guidance/cg90) 2009 (updated 2016).
s1 s2 s3	Depression	**Control: Depression ever.** Not endorsing depression or screening positive on PHQ or CIDI	NOT (reported diagnosis of depression 20544 or 20002) AND NOT Core symptoms from above AND PHQ score ≤5	Case plus control plus subthreshold should include all participants with valid responses. By excluding subthreshold symptoms, we can be confident that this group has not experienced a classical depressive episode
s1 s2 s3	Depression	**Case: Depression single episode.**	Case {depression ever} AND Number of episodes (20442)=1 AND NOT case {bipolar type I} Excluded if number of episodes missing or bipolar state missing	Single episode, recurrent depression and bipolar type I should include all depression cases with valid responses
s1 s2 s3	Depression	**Case: Recurrent depression.**	{depression ever} AND Number of episodes (20442) >1 or -999 (too many to count) AND NOT case {bipolar type I} Excluded if number of episodes missing or bipolar state missing	Single episode, recurrent depression and bipolar type I should include all depression cases with valid responses
nil	Depression	***Variant: Depression single episode triggered by loss***	{depression single episode} AND worst depression start within two months of traumatic event (20447) = yes	Cases of single episode triggered by loss could be selectively excluded for some analyses, although likely to exclude some true cases of major depressive episode
s3	Depression	**Score: PHQ-9.** score items 0-4 and sum (Little interest or pleasure in doing things 20514, Feeling down, depressed, or hopeless 20510, Trouble sleeping 20517, Feeling tired 20519, Poor appetite or overeating 20511, Feeling bad about yourself 20507, Trouble concentrating 20508, Moving or speaking slowly or fidgety or restless	("20514, 20510, 20517, 20519, 20511, 20507, 20508, 20518, 20513") (subtract 9 if items scored 1-5) If value missing, count as "0" when scoring 0-4	*Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59.*

		20518, Thoughts that you would be better off dead 20513)		
nil	Depression	**Case: Current depression.**		
		PHQ +ve and CIDI+ve Reports symptoms in the last two weeks that have bothered them. Current depression is indicated by five or more items marked to bother at or above a certain intensity: "more than half of days" for first eight items, "some days" for last item.	{depression ever} AND Total symptoms endorsed as occurring more than half days (or some or more days for last item) ≥ 5 • Little interest or pleasure in doing things 20514, Feeling down, depressed, or hopeless 20510, Trouble sleeping 20517, Feeling tired 20519, Poor appetite or overeating 20511, Feeling bad about yourself 20507, Trouble concentrating 20508, Moving or speaking slowly or fidgety or restless 20518, Thoughts that you would be better off dead 20513	For identifying likely depression, can use "diagnostic algorithm" based on DSM criteria, alternatively total score. This is using "diagnostic algorithm" *Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*
nil	Depression	**Control: Current depression.**		
		PHQ score ≤5	PHQ score ≤5	A score of above 5 on PHQ can be used as a cut-off for mild depression. Therefore this control group excludes people with possible mild depression, as well as those who meet full criteria in the diagnostic algorithm. *Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*
nil	Depression	***Variant: Current severe depression*** *As current depression (above) with PHQ score > 15*	{depression current} AND PHQ score >15	*Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*
4 5	Mania	**Symptoms: Hypomania / Mania.** Endorses features of hypomania / mania lasting for a week or more, whether or not they were disruptive, and whether or not a depression ever case. Requires "High-hyper" plus three other symptoms or "Irritable" plus four other symptoms	High/Hyper 20501 = 01 OR Irritable 20502 = 01 AND Four features from: • High/Hyper 20501; Active 20548(01); Talkative 20548(02); Less sleep 20548(03); Creative/ideas	Based on DSM-IV definition of hypo/mania. This includes likely cases of bipolar affective disorder type I, possible bipolar type II (where symptoms last a week), recurrent mania without clear depression, and antidepressant-induced symptoms of hypomania / mania.

			20548(04); Restless 20548(5); Confident 20548(6); Thoughts racing 20548(7); Easily distracted 20548(8) AND Duration 20492 = A week or more	*Smith DJ, Nicholl BI, Cullen B, Martin D, Ul-Haq Z, Evans J, et al. Prevalence and characteristics of probable major depression and bipolar disorder within UK biobank: cross-sectional study of 172,751 participants. PLoS One. 2013;8(11):e75362*
6 s1 s2 s3	Mania	**Case: Bipolar affective disorder type I.** Ever manic/hyper or irritable, plus at least three other features (four if never manic/hyper), plus duration a week or more, plus symptoms caused significant problems. Requires also to be case for depression ever.	Case {depression ever} AND High/Hyper 20501 = 01 OR Irritable 20502 = 01 AND Four features from: • High/Hyper 20501; Active 20548(01); Talkative 20548(02); Less sleep 20548(03); Creative/ideas 20548(04); Restless 20548(5); Confident 20548(6); Thoughts racing 20548(7); Easily distracted 20548(8) AND Duration 20492 = A week or more AND Symptoms caused problem 20493 = yes	Case for depression is not required in DSM-IV diagnostic criteria, but is added here to improve the positive predictive value of the test (see text and references). This definition does not exclude antidepressant-induced mania. *Cerimele et al. The prevalence of bipolar disorder in primary care samples: a systematic review, General Hospital Psychiatry 36 (2014) 19-25* *Carvalho, A. F., Y. Takwoingi, et al. (2015). "Screening for bipolar spectrum disorders: a comprehensive meta-analysis of accuracy studies." Journal of affective disorders **172**: 337-346*
nil	Mania	***Variant: Case bipolar type II*** *As above, without disruption from symptoms*	*Case {depression ever}* *AND* *High/Hyper 20501 = 01 OR Irritable 20502 = 01* *AND* *Four features as above* *AND* *Duration 20492 = A week or more*	There is less agreement over the definition of bipolar affective disorder type II. DSM-IV criteria require symptoms for four days or more. Here is one week, so could be predicted to miss some cases.
nil	Mania	**Control: Hypomania / Mania** Not included in hypomania / mania symptoms, nor categorised as bipolar on last UKB classification, nor self-reported bipolar	NOT {hypomania/mania} AND NOT {categorised bipolar on last UKB categorisation 20126 = 1 or 2}	

			AND NOT {self-reported bipolar 20544=10}	
Anxiety				
4	GAD	**Case: GAD Ever.**		
5 6 s2		Excessive worrying about a number of issues, occurring most days for six months and difficult to control, with three or more somatic symptoms and functional impairment.	Worried tense of anxious (20421) = Yes AND Duration (20420) >= 6 months or All my life AND Most days (20538) = Yes AND Excessive: More than most (20425) OR Stronger than most (20542) AND Number of issues: More than one thing (20543) OR Different worries (20540) AND Difficult to control: Difficult to stop worrying (20541) OR Couldn't put it out of mind (20539) OR Difficult to control (20537) AND Functional impairment: Role interference (20418) = Some or A lot AND 3 somatic symptoms out of: Restless. 20426; Keyed up or on edge. 20423; Easily tired. 20429; Having difficulty keeping your mind on what you were doing. 20419; More irritable than usual. 20422; Having tense, sore, or aching muscles. 20417; Often having trouble falling or staying asleep. 20427	CIDI-SF (Composite International Diagnostic Interview – Short Form), GAD module, lifetime version. Scored based on DSM definition of GAD *Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). Int J Methods Psychiatr Res. 1998;7(4):171-85.* *National Institute for Health and Clinical Excellence. Generalised anxiety disorder and panic disorder in adults: management. NICE Clinical Guideline CG113 (available at https://www.nice.org.uk/guidance/cg113) 2011*
nil	GAD	**Control: GAD ever.**		
		Not meeting criteria for GAD ever nor scoring over low cut-off for GAD-7	NOT case {GAD ever} AND GAD-7 score < 5	Excluding those that screen positive for mild anxiety means that there is greater confidence that this group have not had anxiety disorder
s3	GAD	**Score: GAD-7**		

		Score 0-3 and sum a) Feeling nervous, anxious or on edge 20506 b) Not being able to stop or control worrying 20509 c) Worrying too much about different things 20520 d) Trouble relaxing 20515 e) Being so restless that it is hard to sit still 20516 f) Becoming easily annoyed or irritable 20505 g) Feeling afraid as if something awful might happen 20512	Sum {Feeling nervous, anxious or on edge 20506, Not being able to stop or control worrying 20509, Worrying too much about different things 20520, Trouble relaxing 20515, Being so restless that it is hard to sit still 20516, Becoming easily annoyed or irritable 20505, Feeling afraid as if something awful might happen 20512} 0,1,2,3 (nb in biobank coded 1-4, subtract 7 to adjust) If item missing, score 0 when scoring 0-3	*Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59*
nil	GAD	**Case: Current anxiety.**		
		GAD-7 score ≥10 and case GAD ever	Case {GAD ever} AND GAD-7 score ≥10 Where each item scored 0-3	Can be scored with cut-offs for mild, moderate and severe, with cut-offs at 5, 10 and 15. 10 chosen to represent moderate. *Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59*
nil	PTSD	**Score: PCL-6**		
		Sum of scores on questions representing the core symptoms of PTSD Score 1-5 and sum 20497Repeated disturbing thoughts of stressful experience in past month 20498Felt very upset when reminded of stressful experience in past month 20495Avoided activities or situations because of previous stressful experience in past month 20496Felt distant from other people in past month 20494Felt irritable or had angry outbursts in past month 20508 Trouble concentrating (scored 1-4)	Sum {20497Repeated disturbing thoughts of stressful experience in past month, 20498Felt very upset when reminded of stressful experience in past month, 20495Avoided activities or situations because of previous stressful experience in past month, 20496Felt distant from other people in past month, 20494Felt irritable or had angry outbursts in past month} 1,2,3,4,5 + {20508 Trouble concentrating} 1,2,3,4 (nb biobank coded 0-4, subtract 5 to adjust)	Using PHQ item for concentration, scores out of 29 (conventionally scores out of 30), and will make it slightly harder to reach conventional threshold. *Lang AJ, Stein MB. An abbreviated PTSD checklist for use as a screening instrument in primary care. Behaviour research and therapy. 2005;43(5):585-94*
4	PTSD	**Case: PTSD.**		

5 s2		PCL-6 sum of scores 14 or greater is positive screen	(20497Repeated disturbing thoughts + 20498Felt very upset when reminded + 20495Avoided activities or situations + 20496Felt distant + 20494Felt irritable or had angry outbursts + 20508 Trouble concentrating)>13	Does not currently require catastrophic trauma, but refers to "stressful event" in the text of the questions as this is not an exhaustive list of possible trauma.
nil	PTSD	**Control: PTSD.** PCL-6 sum of scores 13 or less is positive screen. Include those who do not complete PCL-6 due to stop rule.	(20497Repeated disturbing thoughts + 20498Felt very upset when reminded + 20495Avoided activities or situations + 20496Felt distant + 20494Felt irritable or had angry outbursts + 20508 Trouble concentrating)>13	
Other symptoms				
4 5 6 s2	Unusual experiences	**Symptom: Unusual experience.** Endorsed possible hallucination or delusion	Heard unreal voice 20463 = yes OR Saw unreal vision 20471 = yes OR Believed unreal conspiracy 20468 = yes OR Believed unreal communication or signs 20474 = yes	Adapted by group from CIDI questions *Nuevo R, Chatterji S, Verdes E, Naidoo N, Arango C, Ayuso-Mateos JL. The Continuum of Psychotic Symptoms in the General Population: A Cross-national Study. Schizophrenia Bulletin. 2012;38(3):475-85*
nil	Unusual experiences	**Symptom: Recent unusual experience.** Reports hallucination or delusion in the last year	Frequency in last year 20467>0	
nil	Unusual experiences	**Control: Unusual experience.** Not endorsing psychotic illness or reporting symptoms	NOT Endorsed diagnosis 20544 of schizophrenia [2] or other psychotic illness [3] AND NOT {ever hallucination} OR {ever delusion}	
nil	Self-harm	**Case: Life not worth living.** Ever felt life not worth living	20479 life NWL = yes (1 or 2)	
4 5	Self-harm	**Case: Self harm.** Ever harmed self, whether or not meant to die	20480 Self harmed = Yes	
Alcohol and addiction				

s3	Alcohol	**Score: AUDIT**		
		Asks about "in the last year" apart from last two questions. (Note coding on UKB is from 1-5, so requires adjustment) Sum individual scores	PART 1 Hazard: Frequency (scored 0-4) 20414, typical drinks (score 0-4) 20403, six or more drinks (scored 0-4) 20416 PART 2 Dependence: Unable to stop (scored 0-4) 20413, failed to do what expected due to drinking (scored 0-4) 20407, needed to drink first thing (scored 0-4) 20412 PART 3 Harm: Guilt due to drinking (scored 0-4) 20409, unable to remember due to drink (scored 0-4) 20408, injury due to drinking ever (scored 0-2) 20411, advice to cut down ever (scored 0-2) 20405	Can be scored using algorithm or cut-offs, with more literature on the latter approach. Using cut-off of 8 is to indicate likelihood of moderate severity, 16 indicates severe, and lower cut-offs have been used to identify hazardous drinking (as opposed to drinking already causing harm). *Reinert, D. F. and J. P. Allen (2007). "The alcohol use disorders identification test: an update of research findings." Alcoholism: Clinical and Experimental Research 31(2): 185-199*
4	Alcohol	**Case: Alcohol Use Disorder.**		
5 s2		Alcohol use disorder of moderate severity is predicted by score of 8 or more.	{AUDIT score} ≥8	*Babor, T. F., J. C. Higgins-Biddle, et al. (2001). "AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care."*
nil	Alcohol	**Control: Alcohol Use Disorder.** Uses inverse of the algorithmic diagnosis of hazardous drinking from AUDIT, excluding those who reported alcohol addiction in this questionnaire or reported at baseline they had stopped drinking due to illness, on drs advice or as a health precaution	AUDIT –ve ((Drinks alcohol 30414 = 0) OR **(**Typical drinks 20403 = "1 or 2" AND Six or more 20416 = "Never")) AND NOT {ever alcohol dependence} AND NOT reason for reducing amount of alcohol drunk 2664 = "ill health", "doctor's advice"or "health precaution" [1,2or3]	This is particularly strict control group to avoid including participants recovering from alcohol harm/dependence in the definition.
3	Addiction	**Case: Addiction ever.**		
6		Endorses "Ever addicted to any substance or behaviour"	"Ever addicted to any substance or behaviour" 20401=1	
3	Addiction	**Case: Substance addiction.**		
		Endorses ever addicted to alcohol or drugs or medication.	Alcohol 20406 = Yes (1) OR Illicit/recreational drugs = Yes (1) OR Medication = Yes (1)	
nil	Addiction	**Case: Current addiction:**		
		Endorses "addiction or dependence ongoing"	20457=1 or 20504=1 or 20415=1 or 20432=1	
3	Addiction	**Case Alcohol dependence ever.**	20404=1	

		Endorses “physically dependent on alcohol”		
nil	Addiction	**Control: Addiction ever.** Not endorsing addiction, or other indicators of misuse: screening AUDIT in severe alcohol use disorder range or daily use of cannabis	NOT {ever addiction} AND NOT {AUDIT score >16} AND {daily cannabis} defined below	
Exposures				
6 s1	Trauma	**Exposure: Childhood adverse events.** Based on answers to the five questions of Childhood Trauma Screen (CTS), all scored 1-5. A score over the threshold on any question is screen positive.	20489Felt loved as a child ≤3 OR 20488Physically abused by family as a child ≥2 OR 20487Felt hated by family member as a child ≥2 OR 20490Sexually molested as a child ≥2 OR 20491Someone to take to doctor when needed as a child ≤4	CTS takes one question from each domain of the Childhood Trauma Questionnaire. Thresholds taken from thresholds for represented domain. *Walker, E. A., et al. (1999). "Adult health status of women with histories of childhood abuse and neglect." The American Journal of Medicine **107**(4): 332-339*
6 s1	Trauma	**Exposure: Adult adverse events.** Based on answers to the five questions of Adult Trauma Screen (written for this questionnaire), all scored 1-5. A score over the threshold on any question is screen positive.	20522Been in a confiding relationship as an adult ≤3 20523Physical violence by partner or ex-partner as an adult ≥2 20521Belittlement by partner or ex-partner as an adult ≥2 20524Sexual interference by partner or ex-partner without consent as an adult ≥2 20525Able to pay rent/mortgage ≤4	Scoring algorithm based on Childhood Trauma Screen and consensus. Note some overlap with baseline questions included in loneliness score.
6 s1	Trauma	**Exposure: Catastrophic trauma.** Endorsed one or more events from checklist	20531Victim of sexual assault = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20529Victim of physically violent crime = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1}	

			20526Been in serious accident believed to be life-threatening = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20530Witnessed sudden violent death = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20528Diagnosed with life-threatening illness = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20527Been involved in combat or exposed to war-zone = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1}
6	Cannabis	**Exposure: Cannabis ever.**	
s1		Endorsed taking cannabis at least once in life.	20453 Ever taken cannabis >0
6	Cannabis	**Exposure: Cannabis daily.**	
s1		Maximum frequency of taking cannabis when using is every day	20454 frequency = every day {4}
6	Cannabis	**Control: Cannabis ever.**	
s1		Reported no cannabis use	20453 Ever taken cannabis = No {0}
Other			
s3	Wellbeing	**Score: Wellbeing.**	
		Sum last three questions	General happiness 20458{scored 1-6} + Happiness with health 20459{scored 1-6} + Life meaningful 20460 {scored 1-5)
nil	Any	**Case: Any distress.** Endorsing functional impairment or help-seeking due to mental distress, reports diagnosis or screens positive for specific condition	(Ever help for mental distress 20499 = yes) OR (Ever impairing mental distress = yes) OR (Mental health problem diagnosed 20544 = {1-18}) OR Case {Depression ever, GAD ever, Addiction ever, Bipolar ever, Psychotic experiences, PTSD, Self harm ever}

nil	Any	**Control: Any distress.** Not endorsing mental distress or conditions, and screens negative	Ever help for mental distress 20499 = no AND Ever impairing mental distress = yes AND NOT (Mental health problem diagnosed 20544 = {1-18 or -818 or -819}) AND NOT Case {Depression ever, GAD ever, Addiction ever, Bipolar ever, Psychotic experiences, PTSD Self harm ever}	Inverse of case. Case plus control will contain all participants that had valid results in all sections

Loneliness and Social Isolation are previously described variables based upon answers to baseline questionnaire.

- Social isolation: (1) “Including yourself, how many people are living together in your household? Include those who usually live in the house such as students living away from home during term time, partners in the armed forces or professions such as pilots” (1 point for living alone); (2) “How often do you visit friends or family or have them visit you?” (1 point for friends and family visit less than once a month); and (3) “Which of the following [leisure/social activities] do you engage in once a week or more often?” (1 point for no participation in social activities at least weekly). Total score 2 or 3
- Loneliness: “Do you often feel lonely?” (no=0, yes=1) and “How often are you able to confide in someone close to you?” (0=almost daily to once every few months; 1=never or almost never). Scored 2

Elovainio, M., C. Hakulinen, et al. "Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study." The Lancet Public Health **2**(6): e260-e266.

Appendix 3: UK Biobank Approved Research

Projects involving authors. For more details or more projects please see website http://www.ukbiobank.ac.uk/approved-research-2/

Box s1 UK Biobank research projects registered by authors, ordered by approval number

Approved research: Date, Principal Investigator(s) and approval number	**Stated aims.** • **Select publications**
2014 - Present Andrew McIntosh 4844	1. Identify and describe specific subtypes of depression 2. Identify the causes underlying different types of depression using GWAS and MRI 3. Test whether resistance to depression (i.e. resilience) to depression can be accurately measured. 4. Identify the mechanisms underlying resilience using genetic and brain imaging data. Extension: Look at genetic and environmental risk factors for harmful alcohol consumption • http://www.nature.com/mp/journal/vaop/ncurrent/full/mp2017153a.html?WT.feed_name=subjects_genetics&foxtrotcallback=true • https://www.ncbi.nlm.nih.gov/pubmed/28717197 • https://www.ncbi.nlm.nih.gov/pubmed/28418403
2015-Present Daniel Smith, 3501	Identify genetic associations with chronic pain and to explore how genetic risk factors for chronic pain might overlap with genetic risk factors for depression. • http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002090
2015-Present Daniel Smith, 6553	Identify genetic associations with a) major depression plus mania/bipolar disorder, and b) vulnerability to depression and other negative mood states (as measured by neuroticism score). These aims will be achieved by conducting genome-wide association studies (GWAS), making use of data from the UK Biobank genotyping project. • http://www.nature.com/tp/journal/v6/n4/full/tp201656a.html • http://bjpo.rcpsych.org/content/2/1/38
2015-Present Daniel Smith 7898	Identify genetic associations with cognitive function (specifically prospective memory, pairs matching, fluid intelligence, reaction time, and forward digit span). This the additional wave of web-based cognitive testing that includes a repeat of the baseline tests above, plus two new tests of visual attention (trail-making) and complex processing speed (digit-symbol substitution). • http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0154222

2015-Present Chris Dickens, 8009	We aim to understand the role of inflammation in predicting the development of depression among adults in the UK. Our study will address the following questions. I. Does genetic variation associated with variation in levels of key inflammatory mediators [i.e. interleukin -1beta, interleukin 1 receptor antagonist, interleukin 2, interleukin 6, tumour necrosis factor alpha, interleukin 10, interferon gamma] predict depression: i. In the Biobank population , ii. Among people with chronic physical illness II. Which socio-demographic and other non-genetic risk factors i) predict depression ii) potentially moderate or mediates the association between inflammation and depression.
2015-Present Daniel Smith 8370	Identify genetic associations with blood pressure/hypertension and to explore how genetic risk factors for blood pressure/hypertension might overlap with genetic risk factors for depression. This GWAS study on hypertension will make use of phenotypic and genetic data on all Biobank participants • http://bjp.rcpsych.org/content/208/4/343.abstract
2015-Present Breda Cullen, 11332	Understanding of variation in cognitive performance in adults with behavioural and brain disorders such as depression, bipolar disorder and multiple sclerosis. This research will comprise a series of cross-sectional studies of baseline cognitive data from the UK Biobank resource. • https://www.ncbi.nlm.nih.gov/pubmed/28387438
2016-Present Gerome Breen, 16577 Andrew McIntosh Bill Deakin Daniel Smith Michael O'Donovan Peter Visscher	Identify changes in DNA that increase the risk for psychiatric disorders alone (specifically the internalising disorders: depression, anxiety including OCD, and related disorders), and for these disorders in the presence of co-morbid physical disorders (autoimmune disorders, including rheumatoid arthritis, and non-immune disorders, including type 2 diabetes, migraine, chronic pain, obesity and body-mass index). Understanding how genetics influence psychiatric disorders, and the relationship between psychiatric and physical disorders • http://www.sciencedirect.com/science/article/pii/S0006322316331134
2017 Xavier Caseras, 17044 Daniel Smith	Investigating the association between common and rare genetic variation, and brain anatomy and function. The results from this project should improve our ability to identify biomarkers for mental disorders. Polygenic risk scores and associated pathways will be calculated on the basis of pre-existing GWAS studies, as well as rare pathogenic CNVs identified in the sample. Anatomical grey and white matter measures will be obtained from brain anatomical images. Functional connectivity indices across different established brain networks would be calculated from resting fMRI images. Cognitive test results and appropriate demographic variables will also be considered.

Appendix 4: Output Text for Tables 2-8

Code at http://dx.doi.org/10.17632/kv677c2th4.1 (includes glossary)

Note that "missing" includes people not in case or control categories, e.g. those with subthreshold depression.

Table 2: Characteristics (UK Biobank only)

MHQ Participants

Descriptive Statistics (N=157366)

Age.Group : 45to54	15% (23482)
55to64	33% (51875)
65to74	45% (70136)
75Plus	8% (11873)
Gender	43% (68265)
Ethnicity : White	97% (152143)
Black	1% (1149)
Asian	1% (1338)
Chinese	0% (364)
Mixed	1% (822)
Other	1% (878)
NA	0% (672)
Migrant.Status : 0	93% (145885)
1	7% (11362)
NA	0% (119)
TDI.Tertiles : Most	12% (19310)
Average	31% (49105)

Least	56% (88752)
NA	0% (199)
Highest.Qualification : NoneOfTheAbove	7% (10930)
Other	5% (7949)
GCSE	29% (44911)
ALevel	13% (21077)
Degree	45% (70999)
NA	1% (1500)
SOC.Job.Code.Broad : Managerial.administrative.professional	60% (93670)
Intermediate	8% (12667)
Routine.manual	4% (5574)
NA	29% (45455)
House.Ownership : OwnOutright	55% (86348)
OwnMortgage	38% (60204)
RentSocial	3% (4178)
RentPrivate	2% (3778)
NA	2% (2858)
Income : LessThan18K	12% (19575)
18Kto30K	21% (33151)
30Kto52K	26% (40947)
52Kto100K	23% (36708)
MoreThan100K	7% (11235)
DontKnowRefuse	9% (14625)
NA	1% (1125)
Cohabiting : 0	7% (11646)

1	75% (117669)
NA	18% (28051)
Smoker : Current	7% (11340)
Former	35% (55284)
Never	57% (90365)
PreferNotToAnswer	0% (304)
NA	0% (73)
Longstanding.Illness : 0	70% (110885)
1	28% (43450)
NA	2% (3031)
Diabetes : 0	96% (151843)
1	3% (5236)
NA	0% (287)
Cancer : 0	93% (145866)
1	7% (11102)
NA	0% (398)
Depressed.At.Baseline : 0	77% (120813)
1	20% (31875)
NA	3% (4678)

All Participants

Descriptive Statistics (N=502618)

Age.Group : 45to54	15% (75116)
55to64	30% (150324)
65to74	44% (221335)

75Plus	11% (55843)
Gender	46% (229164)
Ethnicity : White	94% (472231)
Black	2% (8037)
Asian	2% (9839)
Chinese	0% (1574)
Mixed	1% (2909)
Other	1% (4560)
NA	1% (3468)
Migrant.Status : 0	91% (455951)
1	9% (44883)
NA	0% (1784)
TDI.Tertiles : Most	16% (82352)
Average	32% (159474)
Least	52% (260165)
NA	0% (627)
Highest.Qualification : NoneOfTheAbove	17% (85291)
Other	5% (25810)
GCSE	33% (164845)
ALevel	11% (55331)
Degree	32% (161199)
NA	2% (10142)
SOC.Job.Code.Broad : Managerial.administrative.professional	47% (238110)
Intermediate	11% (55528)
Routine.manual	6% (31469)

	NA	35% (177511)
House.Ownership : OwnOutright		52% (259154)
	OwnMortgage	36% (183401)
	RentSocial	6% (30551)
	RentPrivate	3% (15907)
	NA	3% (13605)
Income : LessThan18K		19% (97221)
	18Kto30K	22% (108197)
	30Kto52K	22% (110790)
	52Kto100K	17% (86279)
	MoreThan100K	5% (22933)
	DontKnowRefuse	14% (71178)
	NA	1% (6020)
Cohabiting : 0		8% (42124)
	1	72% (363148)
	NA	19% (97346)
Smoker : Current		11% (52986)
	Former	34% (173091)
	Never	54% (273589)
	PreferNotToAnswer	0% (2060)
	NA	0% (892)
Longstanding.Illness : 0		66% (329319)
	1	32% (159936)
	NA	3% (13363)
Diabetes : 0		94% (473594)
	1	5% (26407)

NA	1% (2617)
Cancer : 0	92% (461219)
1	8% (38622)
NA	1% (2777)
Depressed.At.Baseline : 0	73% (365116)
1	23% (113321)
NA	5% (24181)

Table 3: Self-reported diagnosis (UK Biobank only)

Descriptive Statistics (N=157366)

SRPsychosisAny	0%	(723)
SRSchizophrenia	0%	(157)
SRPsychosisOther	0%	(604)
SRDepression	21%	(33424)
SRManiaBIP	1%	(837)
SRGADandOthers	14%	(22036)
SRPanicAttacks	6%	(8704)
SRAgoraphobia	0%	(599)
SRSocPhobia	1%	(1962)
SROtherPhobia	1%	(2153)
SROCD	1%	(982)
SRPersonalityDisorder	0%	(385)
SREatingDisorderAny	1%	(1851)
SRAnorexiaNervosa	1%	(891)
SRBulimiaNervosa	0%	(503)
SRBingeEating	0%	(707)
SRASD	0%	(223)
SRADHD	0%	(133)
Alcohol.Dependence.Ever : 0	2%	(2489)
1	1%	(946)
NA	98%	(153931)

Addiction.Ever.SelfReport : 0	93% (146221)
1	6% (9386)
NA	1% (1759)
Substance.Addiction.Ever : 0	3% (4380)
1	3% (5002)
NA	94% (147984)
NoSRConditions	66% (103346)
MultipleSRConditions	12% (19400)

Table 4: Operationally defined syndromes

Gender N= 157366

		N	0	1
Depressed.Ever	No	88650	44831	43819
	Yes	37434	25815	11619
	Missing	31282	18455	12827
Wider.Bipolar.Definition	No	153511	87040	66471
	Yes	2396	1288	1108
	Missing	1459	773	686
GAD.Ever	No	96821	49734	47087
	Yes	11111	7404	3707
	Missing	49434	31963	17471
Unusual.Experience.Ever	No	149298	84232	65066
	Yes	7803	4718	3085
	Missing	265	151	114
Self.Harm.Ever	No	150018	83994	66024
	Yes	6872	4770	2102
	Missing	476	337	139
Alcohol.Use.Disorder	No	308	146	162
	Yes	10911	4063	6848
	Missing	146147	84892	61255
PTSD	No	146656	81965	64691
	Yes	10064	6709	3355
	Missing	646	427	219
MH.Questionnaires	No	101796	54280	47516
	Yes	55570	34821	20749
Overall		157366	89101	68265

Table 5: Comorbidity of syndromes

Depressed.Ever N= 126084 , 31282 Missing

		N	0	1
Wider.Bipolar.Definition	No	123134	87883	35251
	Yes	1901	351	1550
	Missing	1049	416	633
GAD.Ever	No	82833	72664	10169
	Yes	9190	746	8444
	Missing	34061	15240	18821
Unusual.Experience.Ever	No	119932	86302	33630
	Yes	5963	2314	3649
	Missing	189	34	155
Self.Harm.Ever	No	120433	87451	32982
	Yes	5338	1098	4240
	Missing	313	101	212
Alcohol.Use.Disorder	No	231	77	154
	Yes	8186	4781	3405
	Missing	117667	83792	33875
PTSD	No	118578	87668	30910
	Yes	7078	705	6373
	Missing	428	277	151
Overall		126084	88650	37434

Wider.Bipolar.Definition N= 155907 , 1459 Missing

		N	0	1
Depressed.Ever	No	88234	87883	351
	Yes	36801	35251	1550
	Missing	30872	30377	495
GAD.Ever	No	96324	95788	536
	Yes	10879	10101	778
	Missing	48704	47622	1082
Unusual.Experience.Ever	No	148126	146369	1757
	Yes	7560	6962	598
	Missing	221	180	41
Self.Harm.Ever	No	148805	146882	1923

```
|                        |Yes    |  6659|  6206| 453|
|                        |Missing|   443|   423|  20|
+------------------------+-------+------+------+----+
|Alcohol.Use.Disorder    |No     |   301|   280|  21|
|                        |Yes    | 10769| 10442| 327|
|                        |Missing|144837|142789|2048|
+------------------------+-------+------+------+----+
|PTSD                    |No     |145513|143787|1726|
|                        |Yes    |  9790|  9133| 657|
|                        |Missing|   604|   591|  13|
+------------------------+-------+------+------+----+
|Overall                 |       |155907|153511|2396|
+------------------------+-------+------+------+----+
GAD.Ever     N= 107932 , 49434 Missing

+------------------------+-------+------+-----+-----+
|                        |       |N     |0    |1    |
+------------------------+-------+------+-----+-----+
|Depressed.Ever          |No     | 73410|72664|  746|
|                        |Yes    | 18613|10169| 8444|
|                        |Missing| 15909|13988| 1921|
+------------------------+-------+------+-----+-----+
|Wider.Bipolar.Definition|No     |105889|95788|10101|
|                        |Yes    |  1314|  536|  778|
|                        |Missing|   729|  497|  232|
+------------------------+-------+------+-----+-----+
|Unusual.Experience.Ever |No     |103365|93870| 9495|
|                        |Yes    |  4424| 2873| 1551|
|                        |Missing|   143|   78|   65|
+------------------------+-------+------+-----+-----+
|Self.Harm.Ever          |No     |104019|94682| 9337|
|                        |Yes    |  3712| 2008| 1704|
|                        |Missing|   201|  131|   70|
+------------------------+-------+------+-----+-----+
|Alcohol.Use.Disorder    |No     |   176|  111|   65|
|                        |Yes    |  6895| 5609| 1286|
|                        |Missing|100861|91101| 9760|
+------------------------+-------+------+-----+-----+
|PTSD                    |No     |103237|95445| 7792|
|                        |Yes    |  4414| 1140| 3274|
|                        |Missing|   281|  236|   45|
+------------------------+-------+------+-----+-----+
|Overall                 |       |107932|96821|11111|
+------------------------+-------+------+-----+-----+
Unusual.Experience.Ever     N= 157101 , 265 Missing

+------------------------+-------+------+------+----+
|                        |       |N     |0     |1   |
+------------------------+-------+------+------+----+
|Depressed.Ever          |No     | 88616| 86302|2314|
|                        |Yes    | 37279| 33630|3649|
```

	Missing	31206	29366	1840
Wider.Bipolar.Definition	No	153331	146369	6962
	Yes	2355	1757	598
	Missing	1415	1172	243
GAD.Ever	No	96743	93870	2873
	Yes	11046	9495	1551
	Missing	49312	45933	3379
Self.Harm.Ever	No	149811	143290	6521
	Yes	6816	5591	1225
	Missing	474	417	57
Alcohol.Use.Disorder	No	304	268	36
	Yes	10882	10114	768
	Missing	145915	138916	6999
PTSD	No	146460	140310	6150
	Yes	9998	8404	1594
	Missing	643	584	59
Overall		157101	149298	7803

Self.Harm.Ever N= 156890 , 476 Missing

		N	0	1
Depressed.Ever	No	88549	87451	1098
	Yes	37222	32982	4240
	Missing	31119	29585	1534
Wider.Bipolar.Definition	No	153088	146882	6206
	Yes	2376	1923	453
	Missing	1426	1213	213
GAD.Ever	No	96690	94682	2008
	Yes	11041	9337	1704
	Missing	49159	45999	3160
Unusual.Experience.Ever	No	148881	143290	5591
	Yes	7746	6521	1225
	Missing	263	207	56
Alcohol.Use.Disorder	No	307	252	55
	Yes	10880	9921	959
	Missing	145703	139845	5858
PTSD	No	146344	141228	5116
	Yes	9945	8226	1719

```
|                          |Missing|   601|   564|  37|
+--------------------------+-------+------+------+----+
|Overall                   |       |156890|150018|6872|
+--------------------------+-------+------+------+----+
Alcohol.Use.Disorder     N= 11219 , 146147 Missing

+--------------------------+-------+-----+---+-----+
|                          |       |N    |0  |1    |
+--------------------------+-------+-----+---+-----+
|Depressed.Ever            |No     | 4858| 77| 4781|
|                          |Yes    | 3559|154| 3405|
|                          |Missing| 2802| 77| 2725|
+--------------------------+-------+-----+---+-----+
|Wider.Bipolar.Definition|No     |10722|280|10442|
|                          |Yes    |  348| 21|  327|
|                          |Missing|  149|  7|  142|
+--------------------------+-------+-----+---+-----+
|GAD.Ever                  |No     | 5720|111| 5609|
|                          |Yes    | 1351| 65| 1286|
|                          |Missing| 4148|132| 4016|
+--------------------------+-------+-----+---+-----+
|Unusual.Experience.Ever |No     |10382|268|10114|
|                          |Yes    |  804| 36|  768|
|                          |Missing|   33|  4|   29|
+--------------------------+-------+-----+---+-----+
|Self.Harm.Ever            |No     |10173|252| 9921|
|                          |Yes    | 1014| 55|  959|
|                          |Missing|   32|  1|   31|
+--------------------------+-------+-----+---+-----+
|Overall                   |       |11219|308|10911|
+--------------------------+-------+-----+---+-----+
                      PTSD      0      1     NA
Alcohol.Use.Disorder
0                            242     66      0
1                           9523   1360     28
NA                        136891   8638    618
PTSD     N= 156720 , 646 Missing

+--------------------------+-------+------+------+-----+
|                          |       |N     |0     |1    |
+--------------------------+-------+------+------+-----+
|Depressed.Ever            |No     | 88373| 87668|  705|
|                          |Yes    | 37283| 30910| 6373|
|                          |Missing| 31064| 28078| 2986|
+--------------------------+-------+------+------+-----+
|Wider.Bipolar.Definition|No     |152920|143787| 9133|
|                          |Yes    |  2383|  1726|  657|
|                          |Missing|  1417|  1143|  274|
+--------------------------+-------+------+------+-----+
|GAD.Ever                  |No     | 96585| 95445| 1140|
|                          |Yes    | 11066|  7792| 3274|
```

```
|                         |Missing| 49069| 43419| 5650|
+-------------------------+-------+------+------+-----+
|Unusual.Experience.Ever |No     |148714|140310| 8404|
|                         |Yes    |  7744|  6150| 1594|
|                         |Missing|   262|   196|   66|
+-------------------------+-------+------+------+-----+
|Self.Harm.Ever           |No     |149454|141228| 8226|
|                         |Yes    |  6835|  5116| 1719|
|                         |Missing|   431|   312|  119|
+-------------------------+-------+------+------+-----+
|Alcohol.Use.Disorder     |No     |   308|   242|   66|
|                         |Yes    | 10883|  9523| 1360|
|                         |Missing|145529|136891| 8638|
+-------------------------+-------+------+------+-----+
|Overall                  |       |156720|146656|10064|
+-------------------------+-------+------+------+-----+
              MH.Questionnaires     0     1    NA
Depressed.Ever
0                                79396  9254     0
1                                    0 37434     0
NA                               22400  8882     0
                         MH.Questionnaires      0      1     NA
Wider.Bipolar.Definition
0                                           101205  52306      0
1                                                0   2396      0
NA                                             591    868      0
         MH.Questionnaires     0     1    NA
GAD.Ever
0                            77857 18964     0
1                                0 11111     0
NA                           23939 25495     0
                        MH.Questionnaires      0      1     NA
Unusual.Experience.Ever
0                                          101731  47567      0
1                                               0   7803      0
NA                                             65    200      0
               MH.Questionnaires      0      1     NA
Self.Harm.Ever
0                                  101603  48415      0
1                                       0   6872      0
NA                                    193    283      0
                     MH.Questionnaires      0      1     NA
Alcohol.Use.Disorder
0                                          124    184      0
1                                            0  10911      0
NA                                      101672  44475      0
     MH.Questionnaires      0      1     NA
PTSD
0                       101382  45274      0
1                            0  10064      0
NA                         414    232      0
```

Table 6: Lifetime occurrence

MH.Questionnaires.Short N= 157366

		N	0	1
Age.Group	45to54	23482	14364	9118
	55to64	51875	33307	18568
	65to74	70136	51705	18431
	75Plus	11873	9376	2497
Gender	No	89101	57556	31545
	Yes	68265	51196	17069
Ethnicity	White	152143	105072	47071
	Black	1149	855	294
	Asian	1338	1018	320
	Chinese	364	283	81
	Mixed	822	496	326
	Other	878	595	283
	Missing	672	433	239
TDI.Tertiles	Most	19310	11783	7527
	Average	49105	32980	16125
	Least	88752	63877	24875
	Missing	199	112	87
Highest.Qualification	NoneOfTheAbove	10930	8088	2842
	Other	7949	5615	2334
	GCSE	44911	31211	13700
	ALevel	21077	14119	6958
	Degree	70999	48700	22299
	Missing	1500	1019	481
SOC.Job.Code.Broad	Managerial.administrative.professional	93670	63860	29810
	Intermediate	12667	8648	4019
	Routine.manual	5574	3936	1638
	Missing	45455	32308	13147
House.Ownership	OwnOutright	86348	63477	22871
	OwnMortgage	60204	39364	20840
	RentSocial	4178	2040	2138
	RentPrivate	3778	2122	1656
	Missing	2858	1749	1109
Income	LessThan18K	19575	12155	7420
	18Kto30K	33151	22709	10442
	30Kto52K	40947	28306	12641
	52Kto100K	36708	25856	10852
	MoreThan100K	11235	8369	2866

```
|                           |DontKnowRefuse                        | 14625| 10610| 4015|
|                           |Missing                               |  1125|   747|  378|
+---------------------------+--------------------------------------+------+------+-----+
|Trauma.Childhood           |No                                    | 82406| 62550|19856|
|                           |Yes                                   | 71244| 43913|27331|
|                           |Missing                               |  3716|  2289| 1427|
+---------------------------+--------------------------------------+------+------+-----+
|Trauma.Adult               |No                                    | 69980| 53938|16042|
|                           |Yes                                   | 80959| 50226|30733|
|                           |Missing                               |  6427|  4588| 1839|
+---------------------------+--------------------------------------+------+------+-----+
|Trauma.Catastrophic        |No                                    | 77540| 57955|19585|
|                           |Yes                                   | 79794| 50771|29023|
|                           |Missing                               |    32|    26|    6|
+---------------------------+--------------------------------------+------+------+-----+
|Loneliness                 |No                                    |145865|101724|44141|
|                           |Yes                                   |  5961|  2976| 2985|
|                           |Missing                               |  5540|  4052| 1488|
+---------------------------+--------------------------------------+------+------+-----+
|Smoker                     |Current                               | 11340|  6235| 5105|
|                           |Former                                | 55284| 36425|18859|
|                           |Never                                 | 90365| 65827|24538|
|                           |PreferNotToAnswer                     |   304|   218|   86|
|                           |Missing                               |    73|    47|   26|
+---------------------------+--------------------------------------+------+------+-----+
|Cannabis.Ever              |No                                    |122479| 88209|34270|
|                           |Yes                                   | 34658| 20397|14261|
|                           |Missing                               |   229|   146|   83|
+---------------------------+--------------------------------------+------+------+-----+
|Moderate.Physical.Activity|No                                     | 18834| 12406| 6428|
|                           |Yes                                   |134178| 93331|40847|
|                           |Missing                               |  4354|  3015| 1339|
+---------------------------+--------------------------------------+------+------+-----+
|Longstanding.Illness       |No                                    |110885| 80489|30396|
|                           |Yes                                   | 43450| 26341|17109|
|                           |Missing                               |  3031|  1922| 1109|
+---------------------------+--------------------------------------+------+------+-----+
|Overall                    |                                      |157366|108752|48614|
+---------------------------+--------------------------------------+------+------+-----+
Neuroticism - MH Screen == 0: Mean, SD
[1] 3.206064
[1] 2.839727
Neuroticism - MH Screen == 1: Mean, SD
[1] 5.371463
[1] 3.347723
                        Cannabis.Daily     0     1    NA
MH.Questionnaires.Short
0                                       19675   868 88209
1                                       12899  1445 34270
NA                                          0     0     0
                        Social.Isolation     0     1    NA
```

```
MH.Questionnaires.Short
0                                     99832  7793  1127
1                                     43121  4970   523
NA                                        0     0     0
Depressed.Ever     N= 126084 , 31282 Missing
```

		N	0	1
Age.Group	45to54	18477	11332	7145
	55to64	41564	26755	14809
	65to74	56539	42800	13739
	75Plus	9504	7763	1741
Gender	No	70646	44831	25815
	Yes	55438	43819	11619
Ethnicity	White	122028	85731	36297
	Black	904	688	216
	Asian	1032	796	236
	Chinese	299	235	64
	Mixed	616	376	240
	Other	679	466	213
	Missing	526	358	168
TDI.Tertiles	Most	14860	9204	5656
	Average	38908	26518	12390
	Least	72158	52837	19321
	Missing	158	91	67
Highest.Qualification	NoneOfTheAbove	8471	6318	2153
	Other	6468	4591	1877
	GCSE	35628	24917	10711
	ALevel	16777	11398	5379
	Degree	57536	40597	16939
	Missing	1204	829	375
SOC.Job.Code.Broad	Managerial.administrative.professional	75554	52495	23059
	Intermediate	9901	6785	3116
	Routine.manual	4329	3157	1172
	Missing	36300	26213	10087
House.Ownership	OwnOutright	69997	52596	17401
	OwnMortgage	47945	31637	16308
	RentSocial	3070	1409	1661
	RentPrivate	2860	1615	1245
	Missing	2212	1393	819
Income	LessThan18K	14972	9219	5753
	18Kto30K	26330	18177	8153
	30Kto52K	32844	23089	9755

```
|                          |52Kto100K                             | 30076|21796| 8280|
|                          |MoreThan100K                          |  9377| 7270| 2107|
|                          |DontKnowRefuse                        | 11567| 8480| 3087|
|                          |Missing                               |   918|  619|  299|
+--------------------------+--------------------------------------+------+-----+-----+
|Trauma.Childhood          |No                                    | 67994|52786|15208|
|                          |Yes                                   | 55367|34223|21144|
|                          |Missing                               |  2723| 1641| 1082|
+--------------------------+--------------------------------------+------+-----+-----+
|Trauma.Adult              |No                                    | 58538|46365|12173|
|                          |Yes                                   | 62695|38802|23893|
|                          |Missing                               |  4851| 3483| 1368|
+--------------------------+--------------------------------------+------+-----+-----+
|Trauma.Catastrophic       |No                                    | 63137|47873|15264|
|                          |Yes                                   | 62927|40761|22166|
|                          |Missing                               |    20|   16|    4|
+--------------------------+--------------------------------------+------+-----+-----+
|Loneliness                |No                                    |117738|83794|33944|
|                          |Yes                                   |  4071| 1704| 2367|
|                          |Missing                               |  4275| 3152| 1123|
+--------------------------+--------------------------------------+------+-----+-----+
|Smoker                    |Current                               |  8715| 5077| 3638|
|                          |Former                                | 43836|29909|13927|
|                          |Never                                 | 73236|53450|19786|
|                          |PreferNotToAnswer                     |   231|  168|   63|
|                          |Missing                               |    66|   46|   20|
+--------------------------+--------------------------------------+------+-----+-----+
|Cannabis.Ever             |No                                    | 98596|71683|26913|
|                          |Yes                                   | 27334|16870|10464|
|                          |Missing                               |   154|   97|   57|
+--------------------------+--------------------------------------+------+-----+-----+
|Moderate.Physical.Activity|No                                    | 14658| 9660| 4998|
|                          |Yes                                   |108110|76721|31389|
|                          |Missing                               |  3316| 2269| 1047|
+--------------------------+--------------------------------------+------+-----+-----+
|Longstanding.Illness      |No                                    | 90636|67421|23215|
|                          |Yes                                   | 33209|19846|13363|
|                          |Missing                               |  2239| 1383|  856|
+--------------------------+--------------------------------------+------+-----+-----+
|Overall                   |                                      |126084|88650|37434|
+--------------------------+--------------------------------------+------+-----+-----+
Neuroticism - Depressed.Ever == 0: Mean, SD
[1] 2.796924
[1] 2.609222
Neuroticism - Depressed.Ever == 1: Mean, SD
[1] 5.574243
[1] 3.336788
GAD.Ever     N= 107932 , 49434 Missing

+--------------------------+--------------------------------------+------+-----+-----+
|                          |                                      |N     |0    |1    |
```

Age.Group	45to54	15395	13047	2348
	55to64	34468	29998	4470
	65to74	49432	45540	3892
	75Plus	8637	8236	401
Gender	No	57138	49734	7404
	Yes	50794	47087	3707
Ethnicity	White	104353	93604	10749
	Black	841	782	59
	Asian	927	839	88
	Chinese	266	250	16
	Mixed	511	438	73
	Other	588	519	69
	Missing	446	389	57
TDI.Tertiles	Most	12537	10681	1856
	Average	33172	29497	3675
	Least	62092	56535	5557
	Missing	131	108	23
Highest.Qualification	NoneOfTheAbove	7812	7157	655
	Other	5566	5070	496
	GCSE	31240	28059	3181
	ALevel	14293	12692	1601
	Degree	48011	42940	5071
	Missing	1010	903	107
SOC.Job.Code.Broad	Managerial.administrative.professional	63787	57187	6600
	Intermediate	8681	7704	977
	Routine.manual	3925	3568	357
	Missing	31539	28362	3177
House.Ownership	OwnOutright	60692	55707	4985
	OwnMortgage	40493	35638	4855
	RentSocial	2539	1912	627
	RentPrivate	2414	2015	399
	Missing	1794	1549	245
Income	LessThan18K	12850	10964	1886
	18Kto30K	22597	20165	2432
	30Kto52K	28220	25325	2895
	52Kto100K	25552	23155	2397
	MoreThan100K	8083	7500	583
	DontKnowRefuse	9869	9036	833
	Missing	761	676	85
Trauma.Childhood	No	59768	55917	3851
	Yes	46060	39129	6931
	Missing	2104	1775	329

Trauma.Adult	No	51832	48672	3160
	Yes	52028	44447	7581
	Missing	4072	3702	370
Trauma.Catastrophic	No	55381	51149	4232
	Yes	52535	45658	6877
	Missing	16	14	2
Loneliness	No	100868	91041	9827
	Yes	3368	2397	971
	Missing	3696	3383	313
Smoker	Current	7476	6282	1194
	Former	37464	33455	4009
	Never	62739	56856	5883
	PreferNotToAnswer	202	181	21
	Missing	51	47	4
Cannabis.Ever	No	85191	77244	7947
	Yes	22617	19476	3141
	Missing	124	101	23
Moderate.Physical.Activity	No	12930	11354	1576
	Yes	92146	82893	9253
	Missing	2856	2574	282
Longstanding.Illness	No	77945	71709	6236
	Yes	28188	23607	4581
	Missing	1799	1505	294
Overall		107932	96821	11111

Neuroticism - GAD.Ever == 0: Mean, SD
[1] 2.91673
[1] 2.66528
Neuroticism - GAD.Ever == 1: Mean, SD
[1] 7.065105
[1] 3.262012
Unusual.Experience.Ever N= 157101 , 265 Missing

		N	0	1
Age.Group	45to54	23447	21962	1485
	55to64	51787	48883	2904
	65to74	70020	67060	2960
	75Plus	11847	11393	454
Gender	No	88950	84232	4718
	Yes	68151	65066	3085

Ethnicity	White	151899	144396	7503
	Black	1144	1092	52
	Asian	1336	1284	52
	Chinese	364	354	10
	Mixed	816	748	68
	Other	874	810	64
	Missing	668	614	54
TDI.Tertiles	Most	19239	17813	1426
	Average	49025	46396	2629
	Least	88639	84911	3728
	Missing	198	178	20
Highest.Qualification	NoneOfTheAbove	10904	10430	474
	Other	7937	7579	358
	GCSE	44833	42693	2140
	ALevel	21044	19932	1112
	Degree	70885	67239	3646
	Missing	1498	1425	73
SOC.Job.Code.Broad	Managerial.administrative.professional	93541	89066	4475
	Intermediate	12646	11980	666
	Routine.manual	5565	5233	332
	Missing	45349	43019	2330
House.Ownership	OwnOutright	86220	82591	3629
	OwnMortgage	60111	57031	3080
	RentSocial	4153	3626	527
	RentPrivate	3764	3437	327
	Missing	2853	2613	240
Income	LessThan18K	19510	18031	1479
	18Kto30K	33083	31433	1650
	30Kto52K	40887	38905	1982
	52Kto100K	36676	35174	1502
	MoreThan100K	11221	10825	396
	DontKnowRefuse	14602	13864	738
	Missing	1122	1066	56
Trauma.Childhood	No	82310	79609	2701
	Yes	71088	66305	4783
	Missing	3703	3384	319
Trauma.Adult	No	69890	67751	2139
	Yes	80794	75510	5284
	Missing	6417	6037	380
Trauma.Catastrophic	No	77441	75079	2362
	Yes	79628	74189	5439
	Missing	32	30	2

Loneliness	No	145632	138675	6957
	Yes	5945	5375	570
	Missing	5524	5248	276
Smoker	Current	11308	10471	837
	Former	55182	52239	2943
	Never	90236	86233	4003
	PreferNotToAnswer	302	285	17
	Missing	73	70	3
Cannabis.Ever	No	122295	117062	5233
	Yes	34577	32020	2557
	Missing	229	216	13
Moderate.Physical.Activity	No	18805	17774	1031
	Yes	133949	127427	6522
	Missing	4347	4097	250
Longstanding.Illness	No	110754	106409	4345
	Yes	43324	40082	3242
	Missing	3023	2807	216
Overall		157101	149298	7803

Neuroticism - Unusual.Experience.Ever == 0: Mean, SD
[1] 3.798856
[1] 3.133143
Neuroticism - Unusual.Experience.Ever == 1: Mean, SD
[1] 5.177402
[1] 3.465169
Addiction.Ever N= 153839 , 3527 Missing

		N	0	1
Age.Group	45to54	22548	20535	2013
	55to64	50439	47011	3428
	65to74	69093	65627	3466
	75Plus	11759	11280	479
Gender	No	87432	82876	4556
	Yes	66407	61577	4830
Ethnicity	White	148768	139731	9037
	Black	1126	1060	66
	Asian	1315	1258	57
	Chinese	356	340	16
	Mixed	784	694	90
	Other	845	791	54
	Missing	645	579	66

TDI.Tertiles	Most	18501	16560	1941
	Average	47870	44524	3346
	Least	87273	83192	4081
	Missing	195	177	18
Highest.Qualification	NoneOfTheAbove	10763	10236	527
	Other	7817	7457	360
	GCSE	44091	41647	2444
	ALevel	20589	19156	1433
	Degree	69113	64582	4531
	Missing	1466	1375	91
SOC.Job.Code.Broad	Managerial.administrative.professional	91412	85683	5729
	Intermediate	12358	11593	765
	Routine.manual	5409	4995	414
	Missing	44660	42182	2478
House.Ownership	OwnOutright	85001	81085	3916
	OwnMortgage	58515	54418	4097
	RentSocial	3961	3328	633
	RentPrivate	3594	3118	476
	Missing	2768	2504	264
Income	LessThan18K	19080	17514	1566
	18Kto30K	32479	30487	1992
	30Kto52K	40031	37664	2367
	52Kto100K	35787	33649	2138
	MoreThan100K	10962	10309	653
	DontKnowRefuse	14403	13810	593
	Missing	1097	1020	77
Trauma.Childhood	No	81010	77695	3315
	Yes	69239	63439	5800
	Missing	3590	3319	271
Trauma.Adult	No	68937	66162	2775
	Yes	78636	72333	6303
	Missing	6266	5958	308
Loneliness	No	142745	134346	8399
	Yes	5736	5067	669
	Missing	5358	5040	318
Smoker	Current	10572	8656	1916
	Former	53506	48613	4893
	Never	89399	86852	2547
	PreferNotToAnswer	290	269	21
	Missing	72	63	9
Cannabis.Ever	No	121261	116229	5032

```
|                          |Yes                                    | 32377| 28047|4330|
|                          |Missing                                |   201|   177|  24|
+--------------------------+---------------------------------------+------+------+----+
|Moderate.Physical.Activity|No                                     | 18371| 17019|1352|
|                          |Yes                                    |131218|123422|7796|
|                          |Missing                                |  4250|  4012| 238|
+--------------------------+---------------------------------------+------+------+----+
|Longstanding.Illness      |No                                     |108545|102971|5574|
|                          |Yes                                    | 42373| 38785|3588|
|                          |Missing                                |  2921|  2697| 224|
+--------------------------+---------------------------------------+------+------+----+
|Overall                   |                                       |153839|144453|9386|
+--------------------------+---------------------------------------+------+------+----+
Neuroticism - Addiction.Ever == 0: Mean, SD
[1] 3.750988
[1] 3.107305
Neuroticism - Addiction.Ever == 1: Mean, SD
[1] 5.35387
[1] 3.503883
               Trauma.Catastrophic     0     1    NA
Addiction.Ever
0                                  73279 71155    19
1                                   3108  6278     0
NA                                  1153  2361    13
               Cannabis.Daily      0      1     NA
Addiction.Ever
0                              28224      0 116229
1                               3487    867   5032
NA                               863   1446   1218
```

Appendix 5

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Davis et al MHQ paper
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Y
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Y
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Y
Objectives	3	State specific objectives, including any prespecified hypotheses	Y
Methods			
Study design	4	Present key elements of study design early in the paper	Y
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Referenced
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Referenced
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Y - appendix
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Y
Bias	9	Describe any efforts to address potential sources of bias	N – not relevant

Study size	10	Explain how the study size was arrived at	N – not relevant
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Y – appendix
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	N – none used
		(*b*) Describe any methods used to examine subgroups and interactions	N – none used
		(*c*) Explain how missing data were addressed	N – not relevant
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N – not used
		(*e*) Describe any sensitivity analyses	N – not used
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Y
		(b) Give reasons for non-participation at each stage	Y
		(c) Consider use of a flow diagram	Y
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Y
		(b) Indicate number of participants with missing data for each variable of interest	Y – only in appendix
Outcome data	15*	Report numbers of outcome events or summary measures	Y

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Y – no precision given as sample size v large, and felt it would overstate the accuracy to use 95% CI or similar
		(*b*) Report category boundaries when continuous variables were categorized	Y – in appendix
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N – not used
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N – not used
Discussion			
Key results	18	Summarise key results with reference to study objectives	Y
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Y – limitations of data given, less so limitations of analysis
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Y
Generalisability	21	Discuss the generalisability (external validity) of the study results	Y
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Y

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

UK Biobank

Mental health web-based questionnaire

Version 1.2

http://www.ukbiobank.ac.uk/

5th October 2017

This document details the rationale and procedure for administration of the mental health web-based questionnaire for UK Biobank.

Contents

1. Introduction – scientific rationale 1
2. List of contributors 2
3. Content 3
4. Piloting 5
5. Administration 6
6. Generation of derived mental health phenotypes 7
7. References 7
Appendix: Questions and format of the questionnaire 9

1. Introduction – scientific rationale

In January 2015 approximately 50 delegates contributed to a workshop which was held to identify how UK Biobank could be used for researching mental illness. A smaller Expert Working Group was then convened to devise the questionnaire (see Section 2).

Owing to the waxing and waning of symptoms throughout a lifetime and across a spectrum of mental disorders, it was acknowledged that different strategies were required to identify those with life-time experiences of mental disorders. The existing data from the baseline questionnaire was limited, and it was therefore felt important to enrich UK Biobank's phenotyping of mental disorders.

In addition to identifying episodes of mental illness though routine medical records (which UK Biobank has established linkages to), it was agreed that this may not identify many common mental disorders that often do not present to primary or secondary care and often do not receive a formal diagnosis. As such, the Expert Working Group recommended that UK Biobank collect self-reported information that captures symptoms of possible mental disorders using standard validated assessments. The focus was predominantly on the most common disorders – depression and anxiety. It was also recommended that there should be a number of initial screening questionnaires so one can with greater confidence identify a group of participants with no past or present disorders. The group also recommended brief questionnaires on life events, past trauma, childhood exposure and substance use, as major environmental exposures for mental disorders.

Much genetic research in mental health focuses on the comparison of people who have had at least one episode over their life time with those that have not. It was therefore recommended that the questionnaire should capture both current and lifetime mental disorders and symptoms.

The mental health questionnaire is based, in part, on the World Health Organisation's Composite International Diagnostic Interview (CIDI), alongside complementary tools that have been widely used in mental health research and have established validity and reliability. The CIDI forms the basis of many other major research studies, including those contributing to the work of the international Psychiatric Genomics Consortium, in order to promote comparability between studies.

2. List of contributors

Matthew Hotopf, King's College London (Chair)
Katrina Davis, King's College London
Elaine Fox, University of Oxford
Louise Howard, King's College London
Ann John, Swansea University
Rose McCabe, University of Exeter
Andrew McIntosh, University of Edinburgh
Daniel Smith, University of Glasgow
Stan Zammit, Cardiff University

3. Content

The following table provides details of the tools/scales used in mental health questionnaire.

Domain/question topic	Purpose	Source/tool	Notes about source/tool	Reference
A. Screening questions	To comprehensively screen for presence and absence of any mental health condition, by asking about mental health history in three different ways. This will enable comparisons of respondents who are susceptible to mental illness with those who are more resilient.	Bespoke	A list of psychiatric diagnoses is presented to prompt people who may not have thought of their condition as a mental illness.	
B. Current Depression	Maps onto criteria for major depression and indicates likely presence / absence and severity of current depression. This will allow assessments of how depression is related to other illnesses or situations.	Patient Health Questionnaire 9-question version (PHQ-9)	An established research and clinical tool. This includes repeating the four PHQ questions asked at the baseline assessment clinic and some additional questions to enable likely categorical diagnosis of depression and estimation of severity.	Manea L et al (2012)
B. Lifetime Depression	To enable studies in genomics and other areas that require an assessment of whether respondents have ever experienced depression.	CIDI-SF (Composite International Diagnostic Interview – Short Form), depression module, lifetime version	The CIDI is a World Health Organisation (WHO) instrument for mental health surveys. The short-form was derived from the CIDI, and the current lifetime history version was adapted and validated in 4000 people in the USA. Including it allows comparison between the UKB cohort and other cohorts in the international Psychiatric Genetics Consortium.	Kessler RC et al (1998)
B. Lifetime manic symptoms	To identify people that have experienced symptoms that may indicate a bipolar affective disorder, in order to distinguish them from those with unipolar depression	Bespoke	These questions were also included in the baseline assessment clinic for the last one-third of UK Biobank participants.	Smith D et al (2013)
C. Current anxiety disorder	To identify participants with and without anxiety disorders in order to assess the impact of anxiety alongside depression.	Generalised Anxiety Disorder – 7 questions (GAD-7)	A tool commonly used in research and clinical practice with PHQ-9.	Kroenke K et al (2010)

C. Lifetime anxiety disorder	To enable an assessment of the occurrence of anxiety. It adds value to data on the "neuroticism" trait measured at the baseline assessment, as it is able to give a likely diagnosis, separating out subjects whose anxiety became pathological at points during their lives, from those who remained well.	CIDI-SF, anxiety module, lifetime version	The CIDI-SF lifetime version is derived from a World Health Organisation (WHO) instrument for mental health surveys. It allows comparison between the UKB cohort and other cohorts in the international Psychiatric Genetics Consortium.	Kessler RC et al (1998)
D. Addictions	To enable an assessment of a variety of addictions.	Bespoke	Responses to these questions ascertain lifetime and current addictions. The selected addictions were identified from the literature and by consulting the consortium: alcohol, medication including sedatives and painkillers, illicit drugs, and behaviours such as gambling	
E. Alcohol Use	To enable a comprehensive assessment of patterns in alcohol use with a view to defining misuse and addiction.	Alcohol Use Disorders Identification Test (AUDIT)	Developed by the WHO and extensively used and studied.	Reinert DF and Allen JP (2007)
E. Cannabis Use	To enable an assessment of cannabis use.	Bespoke	Two questions that can identify those with casual and heavy cannabis	
F. Unusual experiences	To enable an assessment of unusual experiences that may be markers of tendency towards psychosis or may be a harbinger of neurodegenerative disease.	CIDI, psychosis module, lifetime version, abridged	The CIDI lifetime version is a World Health Organisation (WHO) instrument for mental health surveys. The CIDI questions were adapted for self-report and reduced in number to as few questions as possible to tap into this theme, while making it possible to compare with the World Mental Health Surveys.	McGrath et al (2015)
G. Adverse events in childhood	To allow an assessment of the associations between adverse events in childhood and mental and physical health.	Childhood Trauma Screener – 5 item (CTS-5)	This is the short version of the Childhood Trauma Questionnaire, designed for adults to rate adverse events that may have happened in childhood.	Bellis M et al (2014); Bernstein DP et al (1994); Glaesmer H et al (2013)
G. Adverse events in adult life	To allow an assessment of the associations between adverse events in adult life and mental and physical health.	Bespoke	Using the same structure as the CTS, the questions were adapted from the national crime survey for being a victim of crime and adult domestic violence. Questions were also asked about specific known triggers for post-traumatic stress disorder.	Khalifeh H et al (2015)

G. Post-traumatic stress disorder	To allow an assessment of the occurrence of post-traumatic stress disorder.	Post-traumatic stress disorder Check List – civilian Short version (PCL-S)	Maps onto the DSM-IV criteria and is well-validated.	Wilkins KC et al (2011)
H. Self-harm and suicidal thoughts	To allow an assessment of the frequency of self-harm and suicidal thoughts (with a view to assessing the impact of mental health issues on this outcome).	Bespoke	There were no instruments that were considered adequate, especially in terms of distinguishing between self-harm without suicidal intent and suicide attempts. The working group devised a set of questions, which we have piloted for acceptability.	
J. Subjective wellbeing	To assess the subjective well-being of UK Biobank participants. Included in response to piloting, where participants felt that ending on traumatic experiences and self-harm was uncomfortable.	Bespoke (from existing questions)	Three questions are asked. Two from the UK Biobank baseline assessment provide a euthymic ('positive emotion') aspect of wellbeing and one from the WHO-Quality Of Life (WHOQOL) provides a 'meaning' (eudemonic) measure of wellbeing.	Forgeard MJ et al (2011)
K. Free-text box	To enable participants to add any further information about their mental health status.		Comment box was included in response to piloting, although UK Biobank do not intend to release these comments to researchers at the current time.	
End	Participants are informed that UK Biobank cannot offer help on issues arising. This last page contains links to MIND, survivors trust, victim support, alcohol concern and Samaritans in case they need further support quickly. It also asks them to contact their GP if they would like help with mental health.			

The full list of questions can be found in Appendix 1.

4. Piloting

4.1: The mental health questionnaire underwent small-scale piloting, including among members of a service user advisory group at the National Institute of Health Research Maudsley Biomedical Research Centre to assess acceptability and questionnaire duration for those with multiple mental health episodes.

4.2: The questionnaire also underwent larger-scale piloting in 13,000 volunteers aged 50 years or older who had signed up to the PROTECT study on cognitive ageing http://www.protectstudy.org.uk/default.aspx, funded by the National Institute of Health Research Maudsley Biomedical Research Unit in Dementia.

4.3: Following feedback from these pilot studies, minor modifications were made that including clarifying some questions, providing a comment box at the end for participants to give more detail should they wish to do so, and including links to mental health support networks.

5. Administration

5.1: UK Biobank's re-contact approach for those participants with an email address is as follows:

- an initial invitation email (which included a hyperlink to their personalised questionnaire);
- a reminder email to non-responders sent 2 weeks after the initial invite;
- a reminder send to partial responders (i.e. who only completed part of the questionnaire) 2 weeks after they started the questionnaire;
- a 'last-chance' invitation sent to non-responders 4 months after the initial invite.

5.2: 82% of participants completed the questionnaire in less than 25 minutes.

5.3: Overall, 339,229 participants were sent an email invitation, of whom 158,835 (46.8%) fully completed the questionnaire (as of October 2017). A further 416 participants accessed the questionnaire via the participant website without having received an email invite (because they have not provided UK Biobank with a valid email address).

5.4: Participants for whom we do not have an email address will be encouraged via the annual newsletter (to be sent Q4 2017) to complete the online questionnaire by logging directly onto the participant website.

5.5: Email invitations are also routinely sent to those participants who have recently updated their email address (and who have not yet completed the questionnaire). We therefore anticipate that data will continue to accrue for a small number of participants.

5.6: Please note that UK Biobank has identified a small number of possible mismatches in the linkage of the questionnaire (e.g., where participants who share an email address may have completed their partner's questionnaire). We will release these data once these discrepancies have been resolved.

6. Generation of derived mental health phenotypes

6.1: The Mental Health Expert Working Group (led by Prof Matthew Hotopf, KCL) aim to generate summary derived data-fields related to mental health outcomes, which will be incorporated into the Resource and available for research use in due course.

7. References

Bellis, M. A., et al. National household survey of adverse childhood experiences and their relationship with resilience to health-harming behaviors in England. BMC Medicine, 2014. 12(1): 72.

Bernstein, David P., et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *The American Journal of Psychiatry,* 1994. 151(8): 1132.

Forgeard, M. J., et al. Doing the right thing: Measuring wellbeing for public policy. International Journal of Wellbeing, 2011. 1(1).

Glaesmer H, et al. The childhood trauma screener (CTS)-development and validation of cut-off-scores for classificatory diagnostics. *Psychiatrische Praxis,* 2013. 40(4): p. 220-226.

Kessler RC, et al. The World Health Organization composite international diagnostic interview short-form (CIDI-SF*). International Journal of Methods in Psychiatric Research,* 1998. 7(4): p. 171-185.

Khalifeh, H., et al. Recent intimate partner violence among people with chronic mental illness: findings from a national cross-sectional survey. The British Journal of Psychiatry, 2015. 207(3): 207-212

Kroenke K, et al. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. *General Hospital Psychiatry,* 2010. 32(4): p. 345-59.

Manea L, et al. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. *CMAJ,* 2012. 184(3): p. E191-6.

McGrath JJ, et al. Psychotic Experiences in the General Population: A Cross-National Analysis Based on 31 261 Respondents From 18 Countries. JAMA Psychiatry 2015;72(7):697–705. doi:10.1001/jamapsychiatry.2015.0575

Reinert DF and Allen JP. The alcohol use disorders identification test: an update of research findings. *Alcoholism: Clinical and Experimental Research*, 2007. 31(2): p. 185-199.

Smith DJ et al. Prevalence and characteristics of probable major depression and bipolar disorder within UK Biobank: cross-sectional study of 172,751 participants. *PLoS One*, 2013. 8(11): p. e75362.

Wilkins KC et al., Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian and specific versions. *Depression and Anxiety*, 2011. 28(7): p. 596-606

Appendix: Questions and format of the questionnaire

Introduction
Section A: presence and absence of any mental health condition.
Section B: present and past depression and/or bipolar affective disorder.
Section C: generalised anxiety disorder.
Section D: addictions.
Section E: alcohol and cannabis use.
Section F: unusual and psychotic experiences.
Section G: events in childhood or adult life.
Section H: harm behaviours.
Section J: subjective wellbeing.
End page provides links to support.

Q.No	Field ID	Stem	Responses
Introduction			
INTRO1		We are interested in knowing more about the stresses and strains of life and your mental health. We realise that some of the questions are sensitive and may be difficult to answer but we hope you will feel able to take part. Participating in this questionnaire will help us understand mental health problems like depression and post traumatic stress disorder better. It's important we hear from people who have had these sorts of problems as well as people who have not. Your answers will be kept confidential. None of the information you provide will be sent to your GP or any other agencies.	- Next

	We will not act on any concerns you raise in this questionnaire, and are not able to offer you any help based on the answers you give. However, information on where to find help for the issues in this questionnaire will be shown at the end. Do not worry if you cannot answer a question – you can always press the "prefer not to answer" option and move on.	
Start1	To help you as you work your way through the questionnaire: • Most devices will allow you to click or tap the description beside a choice button to select it **Click or tap on this sentence** **Click /tap here** **and over here** • The progress bar at the bottom of each page (see below) is split into blocks, with each block representing a different section of the questionnaire.	- Next
Identity check	First, we need to check a couple of things.	
ID1 **[no number on implementation]**	Please confirm your month and year of birth	mmm yyyy
ID2 **[no number on implementation]**	Please confirm your sex	[Select one from] - 01 Male - 02 Female
INTRO2	Now let's start with a few general questions about mental distress.	

INTRO2restart		Now let's continue from where you left off…	
Section A: presence and absence of any mental health condition.			
A1	**20500**	In your life, have you suffered from a period of mental distress that prevented you from doing your usual activities?	[Select one from] - 01 Yes - 02 No - UN Do not know - DA Prefer not to answer
A2	**20499**	In your life, did you seek or receive help from a professional (medical doctor, psychologist, social worker, counsellor, nurse, clergy, or other helping professional) for mental distress, psychological problems or unusual experiences?	[Select one from] - 01 Yes - 02 No - UN Do not know - DA Prefer not to answer
A3	**20544**	Have you been diagnosed with one or more of the following mental health problems by a professional, even if you don't have it currently? (tick all that apply): By professional we mean: any doctor, nurse or person with specialist training (such as a psychologist or therapist). Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis.	[Select up to seven from] - 01 Depression - 02 Mania, hypomania, bipolar or manic-depression - 03 Anxiety, nerves or generalized anxiety disorder - 04 Social anxiety or social phobia - 05 Agoraphobia - 06 Any other phobia (eg disabling fear of heights or spiders - 07 Panic attacks - 08 Obsessive compulsive disorder (OCD) - 00 None of the above DA Prefer not to answer

A4	**20544**	Have you been diagnosed with one or more of the following~~,~~ mental health problems by a professional, even if you don't have it currently? (tick all that apply): By professional we mean: any doctor, nurse or person with specialist training (such as a psychologist or therapist). Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis.	[Select up to eight from] - 01 Anorexia nervosa - 02 Bulimia nervosa - 03 Psychological over-eating or binge-eating - 04 Schizophrenia - 05 Any other type of psychosis or psychotic illness - 06 A personality disorder - 07 Autism, Asperger's or autistic spectrum disorder 08 Attention deficit or attention deficit and hyperactivity disorder (ADD/ADHD) - 00 None of the above DA Prefer not to answer
Section B: present and past depression and/or bipolar affective disorder.			
INTRO3		**We next want to ask a few questions about your mood and feelings recently:**	- Next
B1	**a) 20514** **b) 20510** **c) 20534** **d) 20519** **e) 20511** **f) 20507** **g) 20508** **h) 20518** **i) 20513**	Over the last 2 weeks, how often have you been bothered by any of the following problems? a. Little interest or pleasure in doing things b. Feeling down, depressed, or hopeless c. Trouble falling or staying asleep, or sleeping too much d. Feeling tired or having little energy e. Poor appetite or overeating f. Feeling bad about yourself or that you are a failure or have let yourself or your	[Select one from the following for each of the statements] - 01 Not at all - 02 Several days - 03 More than half the days - 04 Nearly every day - DA Prefer not to answer

		family down g. Trouble concentrating on things, such as reading the newspaper or watching television h. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual i. Thoughts that you would be better off dead or of hurting yourself in some way	
BSTEM1		**Now we want to know some more about symptoms in your lifetime**	
B2	**20446**	Have you ever had a time in your life when you felt sad, blue, or depressed for two weeks or more in a row?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
B3	**20441**	Have you ever had a time in your life lasting two weeks or more when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
BSTEM2		Please think of the two-week period in your life when your feelings of depression or loss of interest were worst:	Display throughout following questions B4 to B14
B4	**20447**	Did this worst period start within two months of the death of someone close to you or after a stressful or traumatic event in your life?	[Select one from] - 01 Yes

			- 00 No - DA Prefer not to answer
B5	**20436 (Fraction of day affected)**	How much of the day did these feelings usually last?	- 04 All day long - 03 Most of the day - 02 About half of the day - 01 Less than half of the day - NA Do not know - DA Prefer not to answer
B6	**20439 (Frequency of depressed days)**	Did you feel this way	- 03 Every day - 02 Almost every day - 01 Less often - NA Do not know - DA Prefer not to answer
B7	**20449**	Did you feel more tired out or low on energy than is usual for you?	- 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
B8	**20536**	Did you gain or lose weight without trying, or did you stay about the same weight?	- 01 Gained weight - 02 Lost weight - 03 Both gained and lost some weight during the episode - 00 Stayed about the same or was on a diet

			- NA Do not know - DA Prefer not to answer
B9	**20532**	Did your sleep change?	- 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
B9a		Was that:	[Three questions grouped together, each with forced choice]
	a) 20533	a Trouble falling asleep	- 01 Yes - 00 No
	b) 20535	b Waking too early	
	c) 20534	c Sleeping too much	
B10	**20435**	Did you have a lot more trouble concentrating than usual?	- 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
B11	**20450**	People sometimes feel down on themselves, no good, worthless. Did you feel this way?	- 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
B12	**20437**	Did you think a lot about death – either your own, someone else's or death in general?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer

B13	**20438 (Duration of worst depression)**	About how long altogether did you feel this way? Count the time before, during and after the worst two weeks.	- 01 Less than a month - 02 Between one and three months - 03 Over three months, but less than six months - 04 Over six months, but less than 12 months - 05 One to two years - 06 Over two years - DA Prefer not to answer
B14	**20440**	Think about your roles at the time of this episode, including study / employment, childcare and housework, leisure pursuits. How much did these problems interfere with your life or activities?	- 03 A lot - 02 Somewhat - 01 A little - 00 Not at all - DA Prefer not to answer
BSTEM3		Regarding times in your life when you have had feelings of depression or loss of interest:	Display throughout following questions B15 to B20
B15	**20442**	How many periods did you have in your life lasting two or more weeks where you felt like this?	- 01 One - 02 Several - DA Prefer not to answer
B15a	**20442**	Enter number	BBOX1: Integer box 2 – 999 BBOX1 & “number of times” OR - 01 Too many to count / One episode ran into the next.

B16	**20433**	About how old were you the FIRST time you had a period of two weeks like this? (Whether or not you received any help for it.)	BBOX2: Integer box 2 to current age BBOX2 & "years of age when first felt this way" OR - UN Do not know OR - DA Prefer not to answer
B17	**20445**	Did this episode occur within months of giving birth? Or has it been suggested you had post-natal depression?	- 01 Yes - 00 No - NA Not applicable - UN Do not know - DA Prefer not to answer
B18	**20434**	About how old were you the LAST time you had a period of two weeks like this? (Whether or not you received any help for it)	BBOX3: Integer box 2 to current age BBOX3 & "years of age when last felt this way" Or - UN Don't know Or - DA Prefer not to answer
B19	**20448**	Did you ever tell a professional about these problems (medical doctor, psychologist, social worker, counsellor, nurse, clergy, or other helping professional)?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer

B20	**20546**	Did you ever try the following for these problems? (tick all that apply)	[Select up to three] - 01 Medication prescribed to you (for at least two weeks) - 02 Unprescribed medication (more than once) - 03 Drugs or alcohol (more than once) - 00 None of the above - DA Prefer not to say
B21	**20547**	Did you ever try talking therapies for these problems, or other structured activities you regard as therapeutic? Include only those you attended more than once.	[Select up to two] - 01 Talking therapies, such as psychotherapy, counselling, group therapy or CBT - 02 Other therapeutic activities such as mindfulness, yoga or art classes - 00 None of the above - DA Prefer not to answer
BSTEM4		Now we want to know about some different symptoms.	- Next
B22	**20501**	Have you ever had a period of time when you were feeling so good, “high”, “excited”, or “hyper” that other people thought you were not your normal self or you were so “hyper” that you got into trouble?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
B23	**20502**	Have you ever had a period of time when you were so irritable that you found yourself shouting at people or starting fights or arguments?	- 01 Yes - 00 No - UN Do not know

			- DA Prefer not to answer
B24	**20548**	Please try to remember a period when you were in a “high” or “irritable” state and select all of the following that apply:	[Select up to eight] - 01 I was more active than usual - 02 I was more talkative than usual - 03 I needed less sleep than usual - 04 I was more creative or had more ideas than usual -05 I was more restless than usual -06 I was more confident than usual - 07 My thoughts were racing - 08 I was easily distracted - 00 None of the above - DA Prefer not to answer
B25	**20492**	What is the longest time that these “high” or “irritable” periods have lasted?	[Choose one of] - 01 Less than 24 hours - 02 At least a day, but less than a week - 03 A week or more - UN Do not know - DA Prefer not to answer
B26	**20493**	How much of a problem have these “high” or “irritable” periods caused you?	- 00 No problems - 01 Needed treatment or caused problems with work, relationships, finances, the law or other aspects of life.

			- UN Do not know - DA Prefer not to say
Section C: generalised anxiety disorder.			
INTRO4		We want to know some more about anxiety	Next
C1	**a) 20506** **b) 20509** **c) 20520** **d) 20515** **e) 20516** **f) 20505** **g) 20512**	Over the last 2 weeks, how often have you been bothered by any of the following problems? a) Feeling nervous, anxious or on edge b) Not being able to stop or control worrying c) Worrying too much about different things d) Trouble relaxing e) Being so restless that it is hard to sit still f) Becoming easily annoyed or irritable g) Feeling afraid as if something awful might happen [7 questions on one screen in grid]	[Select one from the following for each of the statements] - 01 Not at all - 02 Several days - 03 More than half the days - 04 Nearly every day - DA Prefer not to answer
C2	**20421**	Have you ever had a period lasting one month or longer when most of the time you felt worried, tense, or anxious?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
C2a	**20420**	What is the longest period of time that this kind of worrying has ever continued?	Cbox2: Integer 0-99 Cbox1: Integer 0-11

			Cbox02 & “year(s) and” & Cbox01 & “month(s)” OR - 03 All my life / as long as I can remember
C3	**20425**	People differ a lot in how much they worry about things. Did you ever have a time when you worried a lot more than most people would in your situation?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
CSTEM1		Please think of the period in your life when you have felt worried, tense, anxious, or more worried than most people would in your situation. This could be in the past, or it could be continuing now.	Display throughout following questions C4 to C10
C4	**20542**	During that period, was your worry stronger than in other people?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
C5	**20538**	Did you worry most days?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
C6	**20543**	Did you usually worry about one particular thing, such as your job security or the failing health of a loved one, or more than one thing?	- 01 One thing - 02 More than one thing - UN Do not know - DA Prefer not to answer
C7	**20541**	Did you find it difficult to stop worrying?	- 01 Yes

			- 00 No - UN Do not know - DA Prefer not to answer
C8	**20540**	Did you ever have different worries on your mind at the same time?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
C9	**20539**	How often was your worry so strong that you couldn't put it out of your mind no matter how hard you tried?	- 03 Often - 02 Sometimes - 01 Rarely - 00 Never - UN Do not know - DA Prefer not to answer
C10	**20537**	How often did you find it difficult to control your worry?	- 03 Often - 02 Sometimes - 01 Rarely - 00 Never - UN Do not know - DA Prefer not to answer
C11	**a) 20426** **b) 20423** **c) 20429** **d) 20419** **e) 20422**	When you were worried or anxious, were you also: a) Restless?	Force choice: - 01 Yes - 02 No

	f) 20417 **g) 20427**	b) Keyed up or on edge? c) Easily tired? d) Having difficulty keeping your mind on what you were doing? e) More irritable than usual? f) Having tense, sore, or aching muscles? g) Often having trouble falling or staying asleep? [Seven questions on one screen]	- NA Do not know For following options:
CSTEM2		Regarding times in your life when you have felt worried, tense or anxious:	Display throughout following questions C12 to C15
C12	**20428**	Did you ever tell a professional about these problems (medical doctor, psychologist, social worker, counsellor, nurse, clergy, or other helping professional)?	- 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
C13	**20549**	Did you ever use the following for the worry or the problems it caused? (tick all that apply): Please include any treatments that you have already told us about under 'depression' if they were also for anxiety:	- 01 Medication prescribed to you (for at least two weeks) - 02 Unprescribed medication (more than once) - 03 Drugs or alcohol (more than once) - 00 None of the above - DA Prefer not to say
C14	**20550**	Did you ever try talking therapies for these problems, or other structured activities you regard as therapeutic? Include only those you attended more than once.	[Select up to two]

		Please include any treatments that you have already told us about under “depression” if they were also for anxiety:	- 01 Talking therapies, such as psychotherapy, counselling, group therapy or CBT - 02 Other therapeutic activities such as mindfulness, yoga or art classes - 00 None of the above - DA Prefer not to answer
C15	**20418**	Think about your roles at the time of this episode, including study / employment, childcare and housework, leisure pursuits. How much did these problems interfere with your life or activities?	[Choose one of] - 03 A lot - 02 Somewhat - 01 A little - 00 Not at all - DA Prefer not to answer
Section D: addictions.			
INTRO5		Now we’d like to ask you a few questions about addiction and dependence	
D1	**20401**	Have you been addicted to or dependent on one or more things, including substances (not cigarettes/coffee) or behaviours (such as gambling)?	[Select one from] - 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
D2	**20406**	Have you been addicted to alcohol?	[Select one from] - 01 Yes - 00 No

			- UN Do not know - DA Prefer not to answer
D2a	**20415**	Is this addiction ongoing?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
D2b	**20404**	Have you been physically dependent on alcohol? This means experiencing withdrawal symptoms, such as sweating, shaking and nausea, if you didn't drink.	[Select one from] - 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
D3	**20503**	Have you been addicted to or dependent on prescription or over-the-counter medication?	[Select one from] - 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
D3a	**20551**	Was this addiction or dependence to one of the following? (tick all that apply)	[Select up to three from] - 01 A sedative, benzodiazepine or sleeping tablet - 02 A painkiller - 00 Something else

			- UN Do not know - DA Prefer not to answer
D3b	**20504**	Is this addiction or dependence ongoing?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
D4	**20456**	Have you been addicted to Illicit or recreational drugs?	[Select one from] - 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
D4a	**20457**	Is this addiction or dependence ongoing?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
D5	**20431**	Have you been addicted to a behaviour (such as gambling) or to anything else we have not mentioned?	[Select one from] - 01 Yes - 00 No - UN Do not know - DA Prefer not to answer
D5a	**20552**	Were you addicted to: (tick all that apply)	[Select up to two from] - 01 A behaviour

			- 02 Something else not mentioned - DA Prefer not to answer
D5b	**20432**	Are these addictions ongoing?	[Select one from] - 01 Yes - 00 No - DA Prefer not to answer
Section E: alcohol and cannabis use.			
INTRO6		Next we would like to ask you about alcohol, as we think it may influence mental health. Your answers will remain confidential so please be honest.	Next
ESTEM1		The next questions are about how frequently you drink alcohol.	Stay on screen for questions E1-E1b
E1	**20414**	How often do you have a drink containing alcohol?	[Choose one from] - 00 Never - 01 Monthly or less - 02 2 to 4 times a month - 03 2 to 3 times a week - 04 4 or more times a week - DA Prefer not to answer
ESTEM2		In the next two questions, a "drink" is defined as one unit of alcohol. Typical units in common alcoholic beverages  Pint or can of beer/lager/cider 2 units  Single shot of spirits (25ml) 1 unit  Small glass of fortified wine 1 unit	Stay on screen for questions E1a and E1b

		 Standard glass of wine (175ml) 2 units  Large glass of wine (250ml) 3 units  Bottle of wine (75cl) 9 units	
E1A	**20403**	How many drinks containing alcohol do you have on a typical day when you are drinking? By “drink” we mean one unit of alcohol.	[Choose one from] - 01 1 or 2 - 02 3 or 4 - 03 5 or 6 - 04 7, 8, or 9 - 05 10 or more - DA Prefer not to answer
E1B	**20416**	How often do you have six or more drinks on one occasion? By “drink” we mean one unit of alcohol.	[Choose one from] - 01 Never - 02 Less than monthly - 03 Monthly - 04 Weekly - 05 Daily or almost daily - DA Prefer not to answer
E2	**20413**	How often during the last year have you found that you were not able to stop drinking once you had started?	[Choose one from] - 00 Never - 01 Less than monthly - 02 Monthly - 03 Weekly

			- 04 Daily or almost daily - DA Prefer not to answer
E3	**20407**	How often during the last year have you failed to do what was normally expected from you because of drinking?	[Choose one from] - 01 Never - 02 Less than monthly - 03 Monthly - 04 Weekly - 05 Daily or almost daily - DA Prefer not to answer
E4	**20412**	How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	[Choose one from] - 01 Never - 02 Less than monthly - 03 Monthly - 04 Weekly - 05 Daily or almost daily - DA Prefer not to answer
E5	**20409**	How often during the last year have you had a feeling of guilt or remorse after drinking?	[Choose from] - 01 Never - 02 Less than monthly - 03 Monthly - 04 Weekly - 05 Daily or almost daily

			- DA Prefer not to answer
E6	**20408**	How often during the last year have you been unable to remember what happened the night before because you had been drinking?	[Choose one from] - 01 Never - 02 Less than monthly - 03 Monthly - 04 Weekly - 05 Daily or almost daily - DA Prefer not to answer
E7	**20411**	Have you or someone else been injured as a result of your drinking?	[Choose one from] - 00 No -01 Yes, but not in the last year - 02 Yes, during the last year - DA Prefer not to answer
E8	**20405**	Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?	[Choose one from] - 00 No - 01 Yes, but not in the last year - 02 Yes, during the last year - DA Prefer not to answer
E8a	**20410**	About how old were you when somebody last commented this way about your drinking habits?	DBOX1: Integer box 2 to current age DBOX1 & “years old” Or - NA Do not know

			- DA Prefer not to answer
ESTEM3		Now we'd like to ask you about cannabis. Your answers will remain confidential	
E9	**20453**	Have you taken CANNABIS (marijuana, grass, hash, ganja, blow, draw, skunk, weed, spliff, dope), even if it was a long time ago?	[Choose one from] - 00 No - 01 Yes, 1-2 times - 02 Yes, 3-10 times - 03 Yes, 11-100 times -04 Yes, more than 100 times - DA Prefer not to answer
E9a	**20454**	Considering when you were taking cannabis most regularly, how often did you take it?	[Choose one from] - 01. Less than once a month - 02. Once a month or more, but not every week - 03. Once a week or more, but not every day - 04. Every day - NA Do not know - DA Prefer not to answer
E9b	**20455**	About how old were you when you last had cannabis?	EBox1: Integer box 2 to current age EBox1 & "years old"
Section F: unusual and psychotic experiences.			
INTRO7		The next set of questions is about unusual experiences that you may have had, like seeing visions or hearing voices. We believe that these things may be quite common,	

		but we don't know for sure. So please take your time and think carefully before answering.	
F1	**20471**	Did you ever see something that wasn't really there that other people could not see? Please do not include any times when you were dreaming or half-asleep or under the influence of alcohol or drugs.	[Choose one from] - 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
F1a	**20473**	About how many times in your life did this happen (when you were not dreaming, not half-asleep, and not under the influence of alcohol or drugs)?	FBOX1: Integer box 1 – 999 FBOX1 & "time(s)" OR - 01 Too many to count - NA Do not know - DA Prefer not to answer
F2	**20463**	Did you ever hear things that other people said did not exist, like strange voices coming from inside your head talking to you or about you, or voices coming out of the air when there was no one around? Please do not include any times when you were dreaming or half-asleep or under the influence of alcohol or drugs.	[Choose one from] - 01 Yes - 00 No - DA Prefer not to say - NA Don't know
F2a	**20465**	About how many times in your life did this happen (when you were not dreaming, not half-asleep, and not under the influence of alcohol or drugs)?	FBOX2: Integer box 1 – 999 FBOX2 & "time(s)" OR - 01 Too many to count

			- NA Do not know - DA Prefer not to answer
F3	**20474**	Did you ever believe that a strange force was trying to communicate directly with you by sending special signs or signals that you could understand but that no one else could understand (for example through the radio or television)? Please do not include any times when you were dreaming or half-asleep or under the influence of alcohol or drugs.	[Choose one from] - 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
F3a	**20476**	About how many times in your life did this happen (when you were not dreaming, not half-asleep, and not under the influence of alcohol or drugs)?	FBOX3: Integer box 1 – 999 FBOX3 & “time(s)” OR - 01 Too many to count - NA Do not know - DA Prefer not to answer
F4	**20468**	Did you ever believe that that there was an unjust plot going on to harm you or to have people follow you, and which your family and friends did not believe existed? Please do not include any times when you were dreaming or half-asleep or under the influence of alcohol or drugs.	[Choose one from] - 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
F4a	**20470**	About how many times in your life did this happen (when you were not dreaming, not half-asleep, and not under the influence of alcohol or drugs)?	FBOX4: Integer box 1 – 999 FBOX4 & “time(s)” OR - 01 Too many to count

			- NA Do not know - DA Prefer not to answer
F5	**20467**	How often did any of these experiences happen in the past 1 year (seeing a vision, hearing a voice, or believing that something strange was trying to communicate with you, or there was a plot against you)?	[Choose one from] - 00 Not at all - 01 Once or twice - 02 Less than once a month - 03 More than once a month - 04 Nearly every day or daily - DA Prefer not to answer
F6	**20461**	How old were you (approximately) when you first had one of these experiences (seeing a vision, hearing a voice, or believing that something strange was trying to communicate with you, or there was a plot against you)?	FBOX5: Integer box 2 to current age FBOX5 & "years old" OR - 01 As long as I can remember - NA Do not know - DA Prefer not to answer
F7	**20462**	How distressing did you find having any of these experiences (seeing a vision, hearing a voice, or believing that something strange was trying to communicate with you, or there was a plot against you)?	[Choose one from] - 00 Not distressing at all, it was a positive experience - 01 Not distressing, a neutral experience - 02 A bit distressing - 03 Quite distressing - 04 Very distressing

			- NA Do not know - DA Prefer not to answer
F8	**20477**	Did you ever talk to a doctor, counsellor, psychiatrist or other health professional about any of these experiences (seeing a vision, hearing a voice, or believing that something strange was trying to communicate with you, or there was a plot against you)?	[Choose one from] - 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
F9	**20466**	Were you ever prescribed a medication by a health professional for any of these experiences (seeing a vision, hearing a voice, or believing that something strange was trying to communicate with you, or there was a plot against you)?	[Choose one from] - 01 Yes - 00 No - NA Do not know - DA Prefer not to answer
Section G: events in childhood or adult life.			
INTRO8		This section asks about your childhood and some possible stresses and strains of life. The answers you give will remain confidential.	
G1	**a) 20489** **b) 20488** **c) 20487** **d) 20490** **e) 20491**	When I was growing up… a) I felt loved b) People in my family hit me so hard that it left me with bruises or marks c) I felt that someone in my family hated me d) Someone molested me (sexually) e) There was someone to take me to the doctor if I needed it	[Select one from] - 00 Never true - 01 Rarely true - 02 Sometimes true - 03 Often - 04 Very often true - DA Prefer not to answer`

		[Five questions on one screen with same options.]	
G2	**a) 20522** **b) 20523** **c) 20521** **d) 20524** **e) 20525**	Since I was sixteen… a) I have been in a confiding relationship b) A partner or ex-partner deliberately hit me or used violence in any other way c) A partner or ex-partner repeatedly belittled me to the extent that I felt worthless d) A partner or ex-partner sexually interfered with me, or forced me to have sex against my wishes e) There was money to pay the rent or mortgage when I needed it [Five questions on one screen with same options.]	[Select one from] - 00 Never true - 01 Rarely true - 02 Sometimes true - 03 Often - 04 Very often true - DA Prefer not to answer
G3	**a) 20531** **b) 20529** **c) 20526** **d) 20530** **e) 20528** **f) 20527**	In your life, have you..? a) Been a victim of a sexual assault, whether by a stranger or someone you knew b) Been attacked, mugged, robbed, or been the victim of a physically violent crime c) Been in a serious accident that you believed to be life-threatening at the time d) Witnessed a sudden violent death (eg. murder, suicide, aftermath of an accident) e) Been diagnosed with a life-threatening illness f) Been involved in combat or exposed to a war-zone (either in the military or as a civilian) [Six questions on one screen with the same options.]	[Select one from] - 00 Never - 01 Yes, but not in the last 12 months - 02 Yes, within the last 12 months - DA Prefer not to answer

G4	**a) 20497** **b) 20498** **c) 20495**	Next is a list of problems and complaints that people sometimes have in response to such extremely stressful experiences. Please indicate how much you have been bothered by that problem in the past month: a) Repeated, disturbing memories, thoughts, or images of a stressful experience? b) Feeling very upset when something reminded you of a stressful experience? c) Avoiding activities or situations because they reminded you of a stressful experience? [Three questions on the same screen with the options]	– [Choose one of] - 00 Not at all - 01 A little bit - 02 Moderately - 03 Quite a bit - 04 Extremely - DA Prefer not to answer
G5	**a) 20496** **b) 20494**	Please indicate how much you have been bothered by that problem in the past month: a) Feeling distant or cut off from other people? b) Feeling irritable or having angry outbursts? [Two questions on the same screen with the options]	[Choose one of] - 00 Not at all - 01 A little bit - 02 Moderately - 03 Quite a bit - 04 Extremely - DA Prefer not to answer
Section H: harm behaviours.			
INTRO9		This section is about thoughts that some people have when they are distressed.	- Next
H1	**20479**	Many people have thoughts that life is not worth living. Have you felt that way?	[Choose one of] - 00 No - 01 Yes, once - 02 Yes, more than once - DA Prefer not to answer

H2	**20485**	Have you contemplated harming yourself (for example by cutting, biting, hitting yourself or taking an overdose)?	[Choose one of] - 00 No - 01 Yes, once - 02 Yes, more than once - DA Prefer not to answer
H2a	**20486**	Have you felt this way in the last 12 months?	[Choose one of] - 00 No - 01 Yes - DA Prefer not to answer
H3	**20480**	Have you deliberately harmed yourself, whether or not you meant to end your life?	[Choose one of] - 00 No - 01 Yes - DA Prefer not to answer
H3a	**20482**	How many times have you harmed yourself?	[Choose one of] - 01 1 - 02 2 - 03 3 or more - DA Prefer not to answer
H3b	**20481**	Have you harmed yourself in the last 12 months, whether or not you meant to end your life?	[Choose one of] - 00 No - 01 Yes - DA Prefer not to answer

H4	**20553**	Have you done any of the following to harm or endanger yourself? (tick all that apply)	[Choose up to five] - 01 Self-injury such as self-cutting, scratching or hitting, etc. - 02 Ingesting a medication in excess of the normal dose - 03 Ingesting alcohol or a recreational or illicit drug - 04 Swallowing dangerous objects or products - 05 Stopping prescribed medication - 00 something not listed - DA Prefer not to answer
H5	**20483**	Have you harmed yourself with the intention to end your life?	[Choose one] - 00 No - 01 Yes - DA Prefer not to answer
H5a	**20484**	Was this in the last 12 months?	[Choose one] - 00 No - 01 Yes - DA Prefer not to answer
H6	**20554**	Following any time when you took an overdose or deliberately tried to harm yourself did you (tick all that apply)	[Choose up to five] - 01 Need hospital treatment (eg A&E)? - 02 See anyone from psychiatric or mental health services, including liaison services?

			- 03 See your GP? - 04 Receive help from friends / family / neighbours? - 05 Use a helpline / voluntary organization? - 00 None of the above - DA Prefer not to answer
Section J: subjective wellbeing.			
INTRO10		Finally we would like to know how you feel about things in general	
J1	**20458**	In general how happy are you?	- 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy -05 Very unhappy - 06 Extremely unhappy - UN Do not know - DA Prefer not to answer
J2	**20459**	In general how happy are you with your HEALTH?	- 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy -05 Very unhappy

			- 06 Extremely unhappy - UN Do not know - DA Prefer not to answer
J3	**20460**	To what extent do you feel your life to be meaningful?	- 01 Not at all - 02 A little - 03 A moderate amount - 04 Very much - 05 An extreme amount - UN Do not know - DA Prefer not to answer
J4		Please use the space below to tell us any further information relevant to this questionnaire. Any information you provide here will not be made available to researchers for research purposes. Please remember that we will not action any concerns you raise in this questionnaire; details of possible sources of support are provided on the next screen [max 1000 characters]. Please note: after you press the Save and finish button below, you will no longer be able to change your answers.	Text box: 1000 characters

Thank you very much for taking the time to complete this questionnaire. Your help is greatly appreciated.

If you feel you need any further help with the issues in this questionnaire, we recommend talking it through with someone you trust, including your GP.

You can find out more about mental health and illness from Mind (www.mind.org.uk). General tips to help you cope with everyday things like money, work, and more are available from: http://www.mind.org.uk/information-support/tips-for-everyday-living/

For support with specific issues, further information is available from:

www.thesurvivorstrust.org (sexual violence)

https://www.victimsupport.org.uk/help-victims (other crime and violence)

https://www.drinkaware.co.uk (alcohol)

http://www.combatstress.org.uk/ (information for military veterans)

http://www.mind.org.uk/news-campaigns/campaigns/bluelight/ (information for emergency service personnel)

https://www.rnli.org/aboutus/lifeguardsandbeaches/Pages/volunteer-lifeguards/support-and-advice.aspx (information for RNLI employees and volunteers).

If you are very upset or do not feel safe, please contact someone as soon as possible. The Samaritans can be contacted on Freephone 116 123, or email jo@samaritans.org. Alternatively, please visit www.samaritans.org

You may now close this browser tab, if you so wish.